

**Title of the Invention**

**CIRCOVIRUS SEQUENCES ASSOCIATED WITH PIGLET  
WEIGHT LOSS DISEASE (PWD)**

**5 Information on Related Applications**

The present application claims the priority benefit, under 35 U.S.C. § 119, of International Application No. PCT/FR98/02634, filed December 4, 1998.

**Background of the Invention**

10 The invention relates to the genomic sequence and nucleotide sequences coding for polypeptides of PWD circovirus, such as the structural and nonstructural polypeptides of said circovirus, as well as vectors including said sequences and cells or animals transformed by these vectors. The invention likewise relates to methods for detecting these nucleic acids or polypeptides and kits for diagnosing infection by  
15 the PWD circovirus. The invention is also directed to a method for selecting compounds capable of modulating the viral infection. The invention further comprises pharmaceutical compositions, including vaccines, for the prevention and/or the treatment of viral infections by PWD circovirus as well as the use of a vector according to the invention for the prevention and/or the treatment of diseases  
20 by gene therapy.

Piglet weight loss disease (PWD), alternatively called fatal piglet wasting (FPW) has been widely described in North America (Harding, J.C., 1997), and authors have reported the existence of a relationship between this pathology and the presence of porcine circovirus (Daft, B. et al., 1996; Clark, E.G., 1997; Harding, J.C., 1997; Harding, J.C. and Clark, E.G., 1997; Nayar, G.P. et al., 1997). A  
25 porcine circovirus has already been demonstrated in established lines of cell cultures derived from pigs and chronically infected (Tischer, I., 1986, 1988, 1995; Dulac, G.C., 1989; Edwards, S., 1994; Allan, G.M., 1995 and McNeilly, F., 1996). This virus, during experimental infection of piglets, does not prove pathogenic for pigs

(Tischer, I., 1986, Horner, G.W., 1991) and its nucleotide sequence has been determined and characterized (Tischer, I., 1982; Meehan, B.M. et al., 1997; Mankertz., A., 1997). The porcine circovirus, called PCV virus, is part of the circovirus genus of the circoviridae family (Murphy, F.A. et al., 1995) whose virion has a circular DNA of size between 1.7 and 2.3 kb, which DNA comprises three open reading frames (ORF1 to ORF3), coding for a replication protein REP involved in the initiation and termination phase of rolling circular replication (RCR) (Heyraud-Nitschke, F., et al., 1995; Harding, M.R. et al., 1993; Hanson, S.F. et al., 1995; Fontes, E.P.B. et al., 1994), coding for a capsid protein (Boulton, L.H. et al., 1997; Hackland, A.F. et al., 1994; Chu, P.W.G. et al., 1993) and coding for a nonstructural protein called a dissemination protein (Lazarowitz., S.G. et al., 1989).

The authors of the present invention have noticed that the clinical signs perceptible in pigs and linked to infection by the PWD circovirus are very distinctive. These manifestations in general appear in pigs of 8 to 12 weeks of age, weaned for 4 to 8 weeks. The first signs are hypotonia without it being possible to speak of prostration. Rapidly (48 hours), the flanks hollow, the line of the spine becomes apparent, and the pigs "blanch." These signs are in general accompanied by hyperthermia, anorexia and most often by respiratory signs (coughing, dyspnea, polypnea). Transitory diarrhea can likewise appear. The disease state phase lasts approximately one month at the end of which the rate of mortality varies from 5 to 20%. To these mortalities, it is expedient to add a variable proportion (5-10%) of cadaveric animals which are no longer able to present an economic future. It is to be noted that outside of this critical stage of the end of post-weaning, no anomaly appears on the farms. In particular, the reproductive function is totally maintained.

On the epidemiological level, the first signs of this pathology appeared at the start of 1995 in the east of the Côtes d'Armor region in France, and the farms affected are especially confined to this area of the region. In December 1996, the number of farms concerned could not be evaluated with precision because of the

absence of a specific laboratory diagnostic method or of an epidemiological surveillance system of the livestock. Based on the clinical facts as well as on results of postmortem examinations supplied by veterinarians, it is possible to estimate this number as several dozen (80-100). The contagiousness of the disease is weak to moderate. Cases are being reported outside the initial area and for the majority are following the transfer of animals coming from farms familiar with the problem. On the other hand, a characteristic of the condition is its strong remanence. Thus, farms which have been affected for a year are still affected in spite of the massive administration of therapeutics. Farms with clinical expression are drawn from various categories of specialization (breeders/fatteners, post-weaners/ fatteners) and different economic structures are concerned. In addition, the disorders appear even in farms where the rules of animal husbandry are respected.

Numerous postmortem examinations have been carried out either on farms or in the laboratory. The elements of the lesional table are disparate. The most constant macroscopic lesions are pneumonia which sometimes appears in patchy form as well as hypertrophy of the lymphatic ganglia. The other lesions above all affect the thoracic viscera including, especially, pericarditis and pleurisy. However, arthritis and gastric ulcers are also observed. The lesions revealed in the histological examination are essentially situated at the pulmonary level (interstitial pneumonia), ganglionic level (lymphoid depletion of the lymph nodes, giant cells) and renal level (glomerulonephritis, vasculitis). The infectious agents have been the subject of wide research. It has been possible to exclude the intervention of pestiviruses and Aujeszky's disease. The disorders appear in the seropositive PDRS (Porcine Dysgenic and Respiratory Syndrome, an infection linked to an arteriovirus) herds, but it has not been possible to establish the role of the latter in the genesis of the disorders (the majority of the farms in Brittany are PDRS seropositive).

The authors of the present invention, with the aim of identifying the etiological agent responsible for PWD, have carried out "contact" tests between piglets which are obviously "ill" and SPF pigs (specific pathogen-free) from

CNEVA (Centre National d'Etudes Vétérinaires et Alimentaires, France). These tests allow the development of signs comparable to those observed on the farm to be observed in protected animal houses. The discrete signs such as moderate hyperthermia, anorexia and intermittent diarrhea appeared after one week of contact. It must be noted that the PDRS virus only diffused subsequent to the clinical signs. In addition, inoculations of organ homogenates of sick animals to healthy pigs allowed signs related to those observed on the farms to be reproduced, although with a lower incidence, linked to the favorable conditions of upkeep of the animals in the experimental installations.

Thus, the authors of the present invention have been able to demonstrate that the pathological signs appear as a well-defined entity affecting the pig at a particular stage of its growth.

This pathology has never been described in France. However, sparse information, especially Canadian, relates to similar facts.

The disorders cannot be mastered with the existing therapeutics.

The data collected both on the farm and by experimentation have allowed the following points to be highlighted:

- PWD is transmissible but its contagiousness is not very high,
- its etiological origin is of infectious and probably viral nature,
- PWD has a persistent character in the affected farms.

Considerable economic consequences ensue for the farms.

Thus, there is currently a significant need for a specific and sensitive diagnostic, whose production is practical and rapid, allowing the early detection of the infection.

A reliable, sensitive and practical test which allows the distinction between strains of porcine circovirus (PCV) is thus strongly desirable.

On the other hand, a need for efficient and well-tolerated treatment of infections with PWD circovirus likewise remains desirable, no vaccine currently being available against PWD circovirus.

Concerning PWD circovirus, it will probably be necessary to understand the role of the immune defense in the physiology and the pathology of the disease to develop satisfactory vaccines.

5 Fuller information concerning the biology of these strains, their interactions with their hosts, the associated infectivity phenomena and those of escape from the immune defenses of the host especially, and finally their implication in the development of associated pathologies, will allow a better understanding of these mechanisms. Taking into account the facts which have been mentioned above and which show in particular the limitations of combatting infection by the PWD  
10 circovirus, it is thus essential today on the one hand to develop molecular tools, especially starting from a better genetic knowledge of the PWD circovirus, and likewise to perfect novel preventive and therapeutic treatments, novel methods of diagnosis and specific, efficacious and tolerated novel vaccine strategies. This is precisely the subject of the present invention.

## 15 **Summary of the Invention**

The present invention relates to vaccines comprising a nucleotide sequence of the genome of Porcine circovirus type B, or a homologue or fragment thereof, and an acceptable pharmaceutical or veterinary vehicle. In one embodiment of the invention, the nucleotide sequence is selected from SEQ ID No. 15, SEQ ID No. 19  
20 SEQ ID No. 23, or SEQ ID No. 25, or a homologue or fragment thereof. In another embodiment of the invention, the homologue has at least 80% sequence identity to SEQ ID No. 15, SEQ ID No. 19, SEQ ID No. 23 or SEQ ID No. 25. In yet another embodiment, the vaccines further comprising an adjuvant

The present invention also relates to vaccines comprising a polypeptide  
25 encoded by a nucleotide sequence of the genome of PCVB, or a homologue or fragment thereof, and an acceptable pharmaceutical or veterinary vehicle. In one embodiment, the homologue has at least 80% sequence identity to SEQ ID No. 15, SEQ ID No. 19, SEQ ID No. 23 or SEQ ID No. 25. In another embodiment of the

invention, the nucleotide sequence is selected from SEQ ID No. 23 or SEQ ID No. 25, or a homologue or fragment thereof. In still another embodiment, the polypeptide has the amino acid sequence of SEQ ID No. 24 or SEQ ID No. 26. In yet another embodiment, the homologue has at least 80% sequence identity to SEQ ID No. 24 or SEQ ID No. 26. In another embodiment, the polypeptide has the amino acid sequence of SEQ ID No. 29, SEQ ID No. 30, SEQ ID No. 31, or SEQ ID No. 32.

A further aspect of the invention relates to vaccines comprising a vector and an acceptable pharmaceutical or veterinary vehicle, the vector comprising a nucleotide sequence of the genome of Porcine circovirus type B, or a homologue or fragment thereof. In one embodiment, the vaccine further comprises a gene coding for an expression product capable of inhibiting or retarding the establishment or development of a genetic or acquired disease.

The present invention also relates to vaccines comprising a cell and an acceptable pharmaceutical or veterinary vehicle, wherein the cell is transformed with a nucleotide sequence of the genome of Porcine circovirus type B, or a homologue or fragment thereof.

Still further, the present invention relates to vaccines comprising a pharmaceutically acceptable vehicle and a single polypeptide, wherein the single polypeptide consists of SEQ ID No. 26.

Additionally, the present invention relates to methods of immunizing a mammal against piglet weight loss disease comprising administering to a mammal an effective amount of the vaccines described above.

These and other aspects of the invention will become apparent to the skilled artisan in view of the teachings contained herein.

**Brief Description of the Drawings**

Figure 1: Experimental scheme which has made it possible to bring about the isolation and the identification of the circovirus associated with PWD of type A and B.

Test 1: experimental reproduction of the PWD by inoculation of pig organ homogenates from farms affected by PWD.

Test 2: experimental reproduction of PWD.

Test 3: experimental reproduction of PWD.

Test 4: no experimental reproduction of PWD.

Figure 2: Organization of the genome of the circovirus associated with PWD of type A (PCVA)

- strand of (+) polarity (SEQ ID No. 1);
- strand of (-) polarity (SEQ ID No. 5, represented according to the orientation 3' → 5');
- sequences of amino acids of proteins encoded by the two DNA strands in the three possible reading frames SEQ ID NOS: 2-4 and 6-8 respectively.

Figure 3: Alignment of the nucleotide sequence SEQ ID No. 1 of the PWD circovirus of type A (PCVA) and of the MEEHAN SEQ ID No. 163 strain and MANKERTZ SEQ ID No. 164 strain circoviruses of the porcine cell lines.

Figure 4: Alignment of the sequence of amino acids SEQ ID No. 10 of a polypeptide encoded by the nucleotide sequence SEQ ID No. 9 (ORF1) of the PWD circovirus of type A (PCVA) and of corresponding nucleotide sequences of the MEEHAN SEQ ID No. 165 strain and MANKERTZ SEQ ID No. 166 strain circoviruses of the porcine cell lines.

Figure 5: Alignment of the sequence of amino acids SEQ ID No. 12 of a polypeptide encoded by the nucleotide sequence SEQ ID No. 11 (ORF2) of the PWD circovirus of type A (PCVA) and of corresponding nucleotide sequences of the MEEHAN SEQ ID No. 167 strain and MANKERTZ SEQ ID No. 168 strain circoviruses of the porcine cell lines.

Figure 6: Alignment of the sequence of amino acids SEQ ID No. 14 of a polypeptide encoded by the nucleotide sequence SEQ ID No. 13 (ORF3) of the PWD circovirus of type A (PCVA) and of corresponding nucleotide sequences of the MEEHAN SEQ ID No. 169 strain and MANKERTZ SEQ ID No. 170 strain circoviruses of the porcine cell lines.

Figure 7: Western blot analysis of recombinant proteins of the PWD circovirus of type A (PCVA).

The analyses were carried out on cell extracts of Sf9 cells obtained after infection with recombinant baculovirus PCF ORF 1.

Figure 8: Organization of the genome of the circovirus associated with the PWD of type B (PCVB)

- strand of (+) polarity (SEQ ID No. 15);
- strand of (-) polarity (SEQ ID No. 19, represented according to the orientation 3' → 5');
- sequence of amino acids of proteins encoded by the two DNA strands in the three possible reading frames SEQ ID NOS: 16-18 and 20-22 respectively.

Figure 9: Evolution of the daily mean gain (DMG) of pig farms affected by piglet weight loss disease (PWD), placed under experimental conditions.



Figure 10: DMG compared for the 3 batches of pigs (F1, F3 and F4) calculated over a period of 28 days, after vaccination test.

Figure 11: Hyperthermia greater than 41°C, expressed as a percentage compared for the 3 batches of pigs (F1, F3 and F4) calculated per week over a period of 28 days, after vaccination test.

Figure 12: Membranes of peptide spots corresponding to the ORF2s revealed with the aid of an infected pig serum, originating from a conventional farm.

The numbers of specific peptides of the circovirus of type B as well as their nonreactive homologs (type A) are indicated in bold.

The nonspecific immunogenic peptides are indicated in italics.

Figure 13: Alignment of amino acid sequences of proteins encoded by the ORF2 of the PWD circovirus of type A SEQ ID No. 12 and by the ORF'2 of the PWD circovirus of type B SEQ ID No. 26. The position of 4 peptides corresponding to specific epitopes of the PWD circovirus of type B is indicated on the corresponding sequence by a bold line, their homolog on the sequence of the PWD circovirus of type A is likewise indicated by an ordinary line.

Figure 14: Charts the results of experiments that demonstrate, in terms of percent hyperthermia, that vaccination with ORF'1 and ORF'2 of PCV-B enhances the level of protection in swine challenged with PCV-B.

Figure 15: Charts the results of experiments that demonstrate, in terms of animal growth, that vaccination with ORF'1 and ORF'2 of PCV-B enhances the level of protection in swine challenged with PCV-B.

**Figure 16:** Immunoperoxidase staining of PK15 cells at 24 h post-transfection with the pcDNA3/ORF'2 plasmid. Expression of PCVB'ORF'2 was confirmed by IPMA following incubation in the presence of the swine anti-PCVB monospecific serum

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### **Detailed Description of the Invention**

The present invention relates to nucleotide sequences of the genome of PWD circovirus selected from the sequences SEQ ID No. 1, SEQ ID No. 5, SEQ ID No. 15, SEQ ID No. 19 or one of their fragments.

10       The nucleotide sequences of sequences SEQ ID No. 1 and SEQ ID No. 5 correspond respectively to the genome sequence of the strand of (+) polarity and of the strand of (-) polarity of the PWD circovirus of type A (or PCVA), the sequence SEQ ID No. 5 being represented according to the orientation 5'→3'.

15       The nucleotide sequences of sequences SEQ ID No. 15 and SEQ ID No. 19 correspond respectively to the genome sequence of the strand of (+) polarity and of the strand of (-) polarity of the PWD circovirus of type B (or PCVB), the sequence SEQ ID No. 19 being represented according to the orientation 5'→3'.

The present invention likewise relates to nucleotide sequences, characterized in that they are selected from:

- 20       a) a nucleotide sequence of a specific fragment of the sequence SEQ ID No. 1, SEQ ID No. 5, SEQ ID No. 15, SEQ ID No. 19 or one of their fragments;
- b) a nucleotide sequence homologous to a nucleotide sequence such as defined in a);
- c) a nucleotide sequence complementary to a nucleotide sequence such as defined in a) or b), and a nucleotide sequence of their corresponding RNA;
- 25       d) a nucleotide sequence capable of hybridizing under stringent conditions with a sequence such as defined in a), b) or c);
- e) a nucleotide sequence comprising a sequence such as defined in a), b), c) or d); and

f) a nucleotide sequence modified by a nucleotide sequence such as defined in a), b), c), d).or e).

Nucleotide, polynucleotide or nucleic acid sequence will be understood according to the present invention as meaning both a double-stranded or single-stranded DNA in the monomeric and dimeric (so-called in tandem) forms and the transcription products of said DNAs.

It must be understood that the present invention does not relate to the genomic nucleotide sequences taken in their natural environment, that is to say in the natural state. It concerns sequences which it has been possible to isolate, purify or partially purify, starting from separation methods such as, for example, ion-exchange chromatography, by exclusion based on molecular size, or by affinity, or alternatively fractionation techniques based on solubility in different solvents, or starting from methods of genetic engineering such as amplification, cloning and subcloning, it being possible for the sequences of the invention to be carried by vectors.

The nucleotide sequences SEQ ID No. 1 and SEQ ID No. 15 were obtained by sequencing of the genome by the Sanger method.

Nucleotide sequence fragment according to the invention will be understood as designating any nucleotide fragment of the PWD circovirus, type A or B, of length of at least 8 nucleotides, preferably at least 12 nucleotides, and even more preferentially at least 20 consecutive nucleotides of the sequence from which it originates.

Specific fragment of a nucleotide sequence according to the invention will be understood as designating any nucleotide fragment of the PWD circovirus, type A or B, having, after alignment and comparison with the corresponding fragments of known porcine circoviruses, at least one nucleotide or base of different nature. For example, the specific nucleotide fragments of the PWD circovirus of type A can easily be determined by referring to Figure 3 of the present invention in which the nucleotides or bases of the sequence SEQ ID No. 1 (circopordfp) are shown which

are of different nature, after alignment of said sequence SEQ ID No. 1 with the other two sequences of known porcine circovirus (circopormeeh and circopormank).

Homologous nucleotide sequence in the sense of the present invention is understood as meaning a nucleotide sequence having at least a percentage identity with the bases of a nucleotide sequence according to the invention of at least 80%, preferably 90% or 95%, this percentage being purely statistical and it being possible to distribute the differences between the two nucleotide sequences at random and over the whole of their length.

Specific homologous nucleotide sequence in the sense of the present invention is understood as meaning a homologous nucleotide sequence having at least one nucleotide sequence of a specific fragment, such as defined above. Said "specific" homologous sequences can comprise, for example, the sequences corresponding to the genomic sequence or to the sequences of its fragments representative of variants of PWD circovirus of type A or B. These specific homologous sequences can thus correspond to variations linked to mutations within strains of PWD circovirus of type A and B, and especially correspond to truncations, substitutions, deletions and/or additions of at least one nucleotide. Said homologous sequences can likewise correspond to variations linked to the degeneracy of the genetic code.

The term "degree or percentage of sequence homology" refers to "degree or percentage of sequence identity between two sequences after optimal alignment" as defined in the present application.

Two amino-acids or nucleotidic sequences are said to be "identical" if the sequence of amino-acids or nucleotidic residues, in the two sequences is the same when aligned for maximum correspondence as described below. Sequence comparisons between two (or more) peptides or polynucleotides are typically performed by comparing sequences of two optimally aligned sequences over a segment or "comparison window" to identify and compare local regions of sequence similarity. Optimal alignment of sequences for comparison may be conducted by the

local homology algorithm of Smith and Waterman, *Ad. App. Math* 2: 482 (1981), by the homology alignment algorithm of Neddleman and Wunsch, *J. Mol. Biol.* 48: 443 (1970), by the search for similarity method of Pearson and Lipman, *Proc. Natl. Acad. Sci. (U.S.A.)* 85: 2444 (1988), by computerized implementation of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by visual inspection.

"Percentage of sequence identity" (or degree or identity) is determined by comparing two optimally aligned sequences over a comparison window, where the portion of the peptide or polynucleotide sequence in the comparison window may comprise additions or deletions (i.e., gaps) as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical amino-acid residue or nucleic acid base occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison and multiplying the result by 100 to yield the percentage of sequence identity.

The definition of sequence identity given above is the definition that would use one of skill in the art. The definition by itself does not need the help of any algorithm, said algorithms being helpful only to achieve the optimal alignments of sequences, rather than the calculation of sequence identity.

From the definition given above, it follows that there is a well defined and only one value for the sequence identity between two compared sequences which value corresponds to the value obtained for the best or optimal alignment.

In the BLAST N or BLAST P "BLAST 2 sequence", software which is available in the web site <http://www.ncbi.nlm.nih.gov/gorf/bl2.html>, and habitually used by the inventors and in general by the skilled man for comparing and determining the identity between two sequences, gap cost which depends on the

sequence length to be compared is directly selected by the software (i.e. 11.2 for substitution matrix BLOSUM-62 for length > 85).

In the present description, PWD circovirus will be understood as designating the circoviruses associated with piglet weight loss disease (PWD) of type A (PCVA) or type B (PCVB), defined below by their genomic sequence, as well as the circoviruses whose nucleic sequences are homologous to the sequences of PWD circoviruses of type A or B, such as in particular the circoviruses corresponding to variants of the type A or of the type B.

Complementary nucleotide sequence of a sequence of the invention is understood as meaning any DNA whose nucleotides are complementary to those of the sequence of the invention, and whose orientation is reversed (antiparallel sequence).

Hybridization under conditions of stringency with a nucleotide sequence according to the invention is understood as meaning a hybridization under conditions of temperature and ionic strength chosen in such a way that they allow the maintenance of the hybridization between two fragments of complementary DNA.

By way of illustration, conditions of great stringency of the hybridization step with the aim of defining the nucleotide fragments described above are advantageously the following.

The hybridization is carried out at a preferential temperature of 65°C in the presence of SSC buffer, 1 × SSC corresponding to 0.15 M NaCl and 0.05 M Na citrate. The washing steps, for example, can be the following:

- 2 × SSC, at ambient temperature followed by two washes with 2 × SSC, 0.5% SDS at 65°C; 2 × 0.5 × SSC, 0.5% SDS; at 65°C for 10 minutes each.

The conditions of intermediate stringency, using, for example, a temperature of 42°C in the presence of a 2 × SSC buffer, or of less stringency, for example a temperature of 37°C in the presence of a 2 × SSC buffer, respectively require a

globally less significant complementarity for the hybridization between the two sequences.

The stringent hybridization conditions described above for a polynucleotide with a size of approximately 350 bases will be adapted by the person skilled in the art for oligonucleotides of greater or smaller size, according to the teaching of  
5 Sambrook et al., 1989.

Among the nucleotide sequences according to the invention, those are likewise preferred which can be used as a primer or probe in methods allowing the homologous sequences according to the invention to be obtained, these methods,  
10 such as the polymerase chain reaction (PCR), nucleic acid cloning and sequencing, being well known to the person skilled in the art.

Among said nucleotide sequences according to the invention, those are again preferred which can be used as a primer or probe in methods allowing the presence of PWD circovirus or one of its variants such as defined below to be diagnosed.

The nucleotide sequences according to the invention capable of modulating, of inhibiting or of inducing the expression of PWD circovirus gene, and/or capable of modulating the replication cycle of PWD circovirus in the host cell and/or organism are likewise preferred. Replication cycle will be understood as designating the invasion and the multiplication of PWD circovirus, and its propagation from  
15 host cell to host cell in the host organism.  
20

Among said nucleotide sequences according to the invention, those corresponding to open reading frames, called ORF sequences, and coding for polypeptides, such as, for example, the sequences SEQ ID No. 9 (ORF1), SEQ ID No. 11 (ORF2) and SEQ ID No. 13 (ORF3) respectively corresponding to the  
25 nucleotide sequences between the positions 47 and 985 determined with respect to the position of the nucleotides on the sequence SEQ ID No. 1, the positions 1723 and 1022 and the positions 658 and 38 with respect to the position of the nucleotides on the sequence SEQ ID No. 5 (represented according to the orientation 3'→5'), the ends being included, or alternatively the sequences SEQ ID No. 23 (ORF'1), SEQ

ID No. 25 (ORF'2) and SEQ ID No. 27 (ORF'3), respectively corresponding to the sequences between the positions 51 and 995 determined with respect to the position of the nucleotides on the sequence SEQ ID No. 15, the positions 1734 and 1033 and the positions 670 and 357, the positions being determined with respect to the position of the nucleotides on the sequence SEQ ID No. 19 (represented according to the orientation 3'→5'), the ends being included, are finally preferred.

The nucleotide sequence fragments according to the invention can be obtained, for example, by specific amplification, such as PCR, or after digestion with appropriate restriction enzymes of nucleotide sequences according to the invention, these methods in particular being described in the work of Sambrook et al., 1989. Said representative fragments can likewise be obtained by chemical synthesis when their size is not very large and according to methods well known to persons skilled in the art.

Modified nucleotide sequence will be understood as meaning any nucleotide sequence obtained by mutagenesis according to techniques well known to the person skilled in the art, and containing modifications with respect to the normal sequences according to the invention, for example mutations in the regulatory and/or promoter sequences of polypeptide expression, especially leading to a modification of the rate of expression of said polypeptide or to a modulation of the replicative cycle.

Modified nucleotide sequence will likewise be understood as meaning any nucleotide sequence coding for a modified polypeptide such as defined below.

The present invention relates to nucleotide sequences of PWD circovirus according to the invention, characterized in that they are selected from the sequences SEQ ID No. 9, SEQ ID No. 11, SEQ ID No. 13, SEQ ID No. 23, SEQ ID No. 25, SEQ ID No. 27 or one of their fragments.

The invention likewise relates to nucleotide sequences characterized in that they comprise a nucleotide sequence selected from:

a) a nucleotide sequence SEQ ID No. 9, SEQ ID No. 11, SEQ ID No. 13, SEQ ID No. 23, SEQ ID No. 25, SEQ ID No. 27 or one of their fragments;



b) a nucleotide sequence of a specific fragment of a sequence such as defined in a);

c) a homologous nucleotide sequence having at least 80% identity with a sequence such as defined in a) or b);

5 d) a complementary nucleotide sequence or sequence of RNA corresponding to a sequence such as defined in a), b) or c); and

e) a nucleotide sequence modified by a sequence such as defined in a), b), c) or d).

10 As far as homology with the nucleotide sequences SEQ ID No. 9, SEQ ID No. 11, SEQ ID No. 13, SEQ ID No. 23, SEQ ID No. 25, SEQ ID No. 27 or one of their fragments is concerned, the homologous, especially specific, sequences having a percentage identity with one of the sequences SEQ ID No. 9, SEQ ID No. 11, SEQ ID No. 13, SEQ ID No. 23, SEQ ID No. 25, SEQ ID No. 27 or one of their fragments of at least 80%, preferably 90% or 95%, are preferred. Said specific  
15 homologous sequences can comprise, for example, the sequences corresponding to the sequences ORF1, ORF2, ORF3, ORF'1, ORF'2 and ORF'3 of PWD circovirus variants of type A or of type B. In the same manner, these specific homologous sequences can correspond to variations linked to mutations within strains of PWD circovirus of type A or of type B and especially correspond to truncations,  
20 substitutions, deletions and/or additions of at least one nucleotide.

Among nucleotide sequences according to the invention, the sequence SEQ ID No. 23 which has a homology having more than 80% identity with the sequence SEQ ID No. 9, as well as the sequence SEQ ID No. 25, are especially preferred.

25 Preferably, the invention relates to the nucleotide sequences according to the invention, characterized in that they comprise a nucleotide sequence selected from the following sequences:

a) SEQ ID No. 33 170 5' TGTTGGCGA 3';

b) SEQ ID No. 34 450 5' AGTTTCCT 3';

c) SEQ ID No. 35 1026 5' TCATTTAGAGGGTCTTTCAG 3';

- d) SEQ ID No. 36 1074 5' GTCAACCT 3';  
e) SEQ ID No. 37 1101 5' GTGGTTGC 3';  
f) SEQ ID No. 38 1123 5' AGCCCAGG 3';  
g) SEQ ID No. 39 1192 5' TTGGCTGG 3';  
5 h) SEQ ID No. 40 1218 5' TCTAGCTCTGGT 3';  
i) SEQ ID No. 41 1501 5' ATCTCAGCTCGT 3';  
j) SEQ ID No. 42 1536 5' TGTCTCCTCCTT 3';  
k) SEQ ID No. 43 1563 5' TCTCTAGA 3';  
l) SEQ ID No. 44 1623 5' TGTACCAA 3';  
10 m) SEQ ID No. 45 1686 5' TCCGTCCT 3';

and their complementary sequences.

In the list of nucleotide sequences a)-m) above, the underlined nucleotides are mutated with respect to the two known sequences of circovirus which are nonpathogenic to pigs. The number preceding the nucleotide sequence represents the position of the first nucleotide of said sequence in the sequence SEQ ID No. 1.

The invention comprises the polypeptides encoded by a nucleotide sequence according to the invention, preferably a polypeptide whose sequence is represented by a fragment, especially a specific fragment, of one of the six sequences of amino acids represented in Figure 2, these six amino acid sequences corresponding to the polypeptides which can be encoded according to one of the three possible reading frames of the sequence SEQ ID No. 1 or of the sequence SEQ ID No. 5, or a polypeptide whose sequence is represented by a fragment, especially a specific fragment, of one of the six sequences of amino acids shown in Figure 8, these six sequences of amino acids corresponding to the polypeptides which can be encoded according to one of the three possible reading frames of the sequence SEQ ID No. 15 or of the sequence SEQ ID No. 19.

The invention likewise relates to the polypeptides, characterized in that they comprise a polypeptide selected from the amino acid sequences SEQ ID No. 10,

SEQ ID No. 12, SEQ ID No. 14, SEQ ID No. 24, SEQ ID No. 26, SEQ ID No. 28 or one of their fragments.

Among the polypeptides according to the invention, the polypeptide of amino acid sequence SEQ ID No. 24 which has a homology having more than 80% identity with the sequence SEQ ID No. 10, as well as the polypeptide of sequence SEQ ID No. 26, are especially preferred.

The invention also relates to the polypeptides, characterized in that they comprise a polypeptide selected from:

- a) a specific fragment of at least 5 amino acids of a polypeptide of an amino acid sequence according to the invention;
- b) a polypeptide homologous to a polypeptide such as defined in a);
- c) a specific biologically active fragment of a polypeptide such as defined in a) or b); and
- d) a polypeptide modified by a polypeptide such as defined in a), b) or c).

Among the polypeptides according to the invention, the polypeptides of amino acid sequences SEQ ID No. 29, SEQ ID No. 30, SEQ ID No. 31 and SEQ ID No. 32 are also preferred, these polypeptides being especially capable of specifically recognizing the antibodies produced during infection by the PWD circovirus of type B. These polypeptides thus have epitopes specific for the PWD circovirus of type B and can thus be used in particular in the diagnostic field or as immunogenic agent to confer protection in pigs against infection by PWD circovirus, especially of type B.

In the present description, the terms polypeptide, peptide and protein are interchangeable.

It must be understood that the invention does not relate to the polypeptides in natural form, that is to say that they are not taken in their natural environment but that they can be isolated or obtained by purification from natural sources, or else

obtained by genetic recombination, or alternatively by chemical synthesis and that they can thus contain unnatural amino acids, as will be described below.

Polypeptide fragment according to the invention is understood as designating a polypeptide containing at least 5 consecutive amino acids, preferably 10  
5 consecutive amino acids or 15 consecutive amino acids.

In the present invention, specific polypeptide fragment is understood as designating the consecutive polypeptide fragment encoded by a specific fragment nucleotide sequence according to the invention.

Homologous polypeptide will be understood as designating the polypeptides  
10 having, with respect to the natural polypeptide, certain modifications such as, in particular, a deletion, addition or substitution of at least one amino acid, a truncation, a prolongation, a chimeric fusion, and/or a mutation. Among the homologous polypeptides, those are preferred whose amino acid sequence has at least 80%, preferably 90%, homology with the sequences of amino acids of  
15 polypeptides according to the invention.

Specific homologous polypeptide will be understood as designating the homologous polypeptides such as defined above and having a specific fragment of polypeptide according to the invention.

In the case of a substitution, one or more consecutive or nonconsecutive  
20 amino acids are replaced by "equivalent" amino acids. The expression "equivalent" amino acid is directed here at designating any amino acid capable of being substituted by one of the amino acids of the base structure without, however, essentially modifying the biological activities of the corresponding peptides and such that they will be defined by the following.

25 These equivalent amino acids can be determined either by depending on their structural homology with the amino acids which they substitute, or on results of comparative tests of biological activity between the different polypeptides, which are capable of being carried out.

By way of example, the possibilities of substitutions capable of being carried out without resulting in an extensive modification of the biological activity of the corresponding modified polypeptides will be mentioned, the replacement, for example, of leucine by valine or isoleucine, of aspartic acid by glutamic acid, of  
5 glutamine by asparagine, of arginine by lysine etc., the reverse substitutions naturally being envisageable under the same conditions.

The specific homologous polypeptides likewise correspond to polypeptides encoded by the specific homologous nucleotide sequences such as defined above and thus comprise in the present definition the polypeptides which are mutated or  
10 correspond to variants which can exist in PWD circovirus, and which especially correspond to truncations, substitutions, deletions and/or additions of at least one amino acid residue.

Specific biologically active fragment of a polypeptide according to the invention will be understood in particular as designating a specific polypeptide  
15 fragment, such as defined above, having at least one of the characteristics of polypeptides according to the invention, especially in that it is:

- capable of inducing an immunogenic reaction directed against a PWD circovirus; and/or
- capable of being recognized by a specific antibody of a polypeptide  
20 according to the invention; and/or
- capable of linking to a polypeptide or to a nucleotide sequence of PWD circovirus; and/or
- capable of exerting a physiological activity, even partial, such as, for example, a dissemination or structural (capsid) activity; and/or
- 25 - capable of modulating, of inducing or of inhibiting the expression of PWD circovirus gene or one of its variants, and/or capable of modulating the replication cycle of PWD circovirus in the cell and/or the host organism.

The polypeptide fragments according to the invention can correspond to isolated or purified fragments naturally present in a PWD circovirus or correspond

to fragments which can be obtained by cleavage of said polypeptide by a proteolytic enzyme, such as trypsin or chymotrypsin or collagenase, or by a chemical reagent, such as cyanogen bromide (CNBr) or alternatively by placing said polypeptide in a very acidic environment, for example at pH 2.5. Such polypeptide fragments can likewise just as easily be prepared by chemical synthesis, from hosts transformed by an expression vector according to the invention containing a nucleic acid allowing the expression of said fragments, placed under the control of appropriate regulation and/or expression elements.

“Modified polypeptide” of a polypeptide according to the invention is understood as designating a polypeptide obtained by genetic recombination or by chemical synthesis as will be described below, having at least one modification with respect to the normal sequence. These modifications will especially be able to bear on amino acids at the origin of a specificity, of pathogenicity and/or of virulence, or at the origin of the structural conformation, and of the capacity of membrane insertion of the polypeptide according to the invention. It will thus be possible to create polypeptides of equivalent, increased or decreased activity, and of equivalent, narrower, or wider specificity. Among the modified polypeptides, it is necessary to mention the polypeptides in which up to 5 amino acids can be modified, truncated at the N- or C-terminal end, or even deleted or added.

As is indicated, the modifications of the polypeptide will especially have as objective:

- to render it capable of modulating, of inhibiting or of inducing the expression of PWD circovirus gene and/or capable of modulating the replication cycle of PWD circovirus in the cell and/or the host organism,
- of allowing its incorporation into vaccine compositions,
- of modifying its bioavailability as a compound for therapeutic use.

The methods allowing said modulations on eukaryotic or prokaryotic cells to be demonstrated are well known to the person skilled in the art. It is likewise well understood that it will be possible to use the nucleotide sequences coding for said

modified polypeptides for said modulations, for example through vectors according to the invention and described below, in order, for example, to prevent or to treat the pathologies linked to the infection.

5 The preceding modified polypeptides can be obtained by using combinatorial chemistry, in which it is possible to systematically vary parts of the polypeptide before testing them on models, cell cultures or microorganisms for example, to select the compounds which are most active or have the properties sought.

Chemical synthesis likewise has the advantage of being able to use:

- 10 - unnatural amino acids, or
- nonpeptide bonds.

Thus, in order to improve the duration of life of the polypeptides according to the invention, it may be of interest to use unnatural amino acids, for example in D form, or else amino acid analogs, especially sulfur-containing forms, for example.

15 Finally, it will be possible to integrate the structure of the polypeptides according to the invention, its specific or modified homologous forms, into chemical structures of polypeptide type or others. Thus, it may be of interest to provide at the N- and C-terminal ends compounds not recognized by the proteases.

20 The nucleotide sequences coding for a polypeptide according to the invention are likewise part of the invention.

The invention likewise relates to nucleotide sequences utilizable as a primer or probe, characterized in that said sequences are selected from the nucleotide sequences according to the invention.

25 Among the pairs of nucleotide sequences utilizable as a pair of primers according to the invention, the pairs of primers selected from the following pairs are preferred:

- a) SEQ ID No. 46 5' GTG TGC TCG ACA TTG GTG TG 3', and  
SEQ ID No. 47 5' TGG AAT GTT AAC GAG CTG AG 3';
- b) SEQ ID No. 46 5' GTG TGC TCG ACA TTG GTG TG 3', and

SEQ ID No. 48 5' CTC GCA GCC ATC TTG GAA TG 3';

c) SEQ ID No. 49 5' CGC GCG TAA TAC GAC TCA CT 3'; and

SEQ ID No. 46 5' GTG TGC TCG ACA TTG GTG TG 3';

d) SEQ ID No. 49 5' CGC GCG TAA TAC GAC TCA CT 3', and

SEQ ID No. 48 5' CTC GCA GCC ATC TTG GAA TG 3'; and

e) SEQ ID No. 50 5' CCT GTC TAC TGC TGT GAG TAC CTT GT 3',

and

SEQ ID No. 51 5' GCA GTA GAC AGG TCA CTC CGT TGT CC  
3'.

The cloning and the sequencing of the PWD circovirus, type A and B, has allowed it to be identified, after comparative analysis with the nucleotide sequences of other porcine circoviruses, that, among the sequences of fragments of these nucleic acids, were those which are strictly specific to the PWD circovirus of type A, of type B or of type A and B, and those which correspond to a consensus sequence of porcine circoviruses other than the PWD circoviruses of type A and/or B.

There is likewise a great need for nucleotide sequences utilizable as a primer or probe specific to the whole of the other known and nonpathogenic porcine circoviruses.

Said consensus nucleotide sequences specific to all circoviruses, other than PWD circovirus of type A and B, are easily identifiable from Figure 3 and the sequence SEQ ID No. 15, and are part of the invention.

Among said consensus nucleotide sequences, that which is characterized in that it is part of the following pair of primers is preferred:

a) SEQ ID No. 46 5' GTG TGC TCG ACA TTG GTG TG 3', and

SEQ ID No. 52 5' TGG AAT GTT AAC TAC CTC AA 3'.

The invention likewise comprises a nucleotide sequence according to the invention, characterized in that said sequence is a specific consensus sequence of



porcine circovirus other than PWD circovirus of type B and in that it is one of the primers of the following pairs of primers:

- a) SEQ ID No. 53     5' GGC GGC GCC ATC TGT AAC GGT TT 3', and  
SEQ ID No. 54     5' GAT GGC GCC GAA AGA CGG GTA TC 3'.

5            It is well understood that the present invention likewise relates to specific polypeptides of known porcine circoviruses other than PWD circovirus, encoded by said consensus nucleotide sequences, capable of being obtained by purification from natural polypeptides, by genetic recombination or by chemical synthesis by procedures well known to the person skilled in the art and such as described in particular below. In the same manner, the labeled or unlabeled mono- or polyclonal  
10            antibodies directed against said specific polypeptides encoded by said consensus nucleotide sequences are also part of the invention.

          It will be possible to use said consensus nucleotide sequences, said corresponding polypeptides as well as said antibodies directed against said  
15            polypeptides in procedures or sets for detection and/or identification such as described below, in place of or in addition to nucleotide sequences, polypeptides or antibodies according to the invention, specific to PWD circovirus type A and/or B.

          These protocols have been improved for the differential detection of the circular monomeric forms of specific replicative forms of the virion or of the DNA  
20            in replication and the dimeric forms found in so-called in-tandem molecular constructs.

          The invention additionally relates to the use of a nucleotide sequence according to the invention as a primer or probe for the detection and/or the amplification of nucleic acid sequences.

25            The nucleotide sequences according to the invention can thus be used to amplify nucleotide sequences, especially by the PCR technique (polymerase chain reaction) (Erlich, 1989; Innis et al., 1990; Rolfs et al., 1991; and White et al., 1997).

These oligodeoxyribonucleotide or oligoribonucleotide primers advantageously have a length of at least 8 nucleotides, preferably of at least 12 nucleotides, and even more preferentially at least 20 nucleotides.

5 Other amplification techniques of the target nucleic acid can be advantageously employed as alternatives to PCR.

The nucleotide sequences of the invention, in particular the primers according to the invention, can likewise be employed in other procedures of amplification of a target nucleic acid, such as:

- 10 - the TAS technique (Transcription-based Amplification System), described by Kwoh et al. in 1989;
- the 3SR technique (Self-Sustained Sequence Replication), described by Guatelli et al. in 1990;
- the NASBA technique (Nucleic Acid Sequence Based Amplification), described by Kievitis et al. in 1991;
- 15 - the SDA technique (Strand Displacement Amplification) (Walker et al., 1992);
- the TMA technique (Transcription Mediated Amplification).

The polynucleotides of the invention can also be employed in techniques of amplification or of modification of the nucleic acid serving as a probe, such as:

- 20 - the LCR technique (Ligase Chain Reaction), described by Landegren et al. in 1988 and improved by Barany et al. in 1991, which employs a thermostable ligase;
- the RCR technique (Repair Chain Reaction), described by Segev in 1992;
- the CPR technique (Cycling Probe Reaction), described by Duck et al. in 25 1990;
- the amplification technique with Q-beta replicase, described by Miele et al. in 1983 and especially improved by Chu et al. in 1986, Lizardi et al. in 1988, then by Burg et al. as well as by Stone et al. in 1996.

In the case where the target polynucleotide to be detected is possibly an RNA, for example an mRNA, it will be possible to use, prior to the employment of an amplification reaction with the aid of at least one primer according to the invention or to the employment of a detection procedure with the aid of at least one probe of the invention, an enzyme of reverse transcriptase type in order to obtain a cDNA from the RNA contained in the biological sample. The cDNA obtained will thus serve as a target for the primer(s) or the probe(s) employed in the amplification or detection procedure according to the invention.

The detection probe will be chosen in such a manner that it hybridizes with the target sequence or the amplicon generated from the target sequence. By way of sequence, such a probe will advantageously have a sequence of at least 12 nucleotides, in particular of at least 20 nucleotides, and preferably of at least 100 nucleotides.

The invention also comprises the nucleotide sequences utilizable as a probe or primer according to the invention, characterized in that they are labeled with a radioactive compound or with a nonradioactive compound.

The unlabeled nucleotide sequences can be used directly as probes or primers, although the sequences are generally labeled with a radioactive element ( $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^3\text{H}$ ,  $^{125}\text{I}$ ) or with a nonradioactive molecule (biotin, acetylaminofluorene, digoxigenin, 5-bromodeoxyuridine, fluorescein) to obtain probes which are utilizable for numerous applications.

Examples of nonradioactive labeling of nucleotide sequences are described, for example, in French Patent No. 78.10975 or by Urdea et al. or by Sanchez-Pescador et al. in 1988.

In the latter case, it will also be possible to use one of the labeling methods described in patents FR-2 422 956 and FR-2 518 755.

The hybridization-technique can be carried out in various manners (Matthews et al., 1988). The most general method consists in immobilizing the nucleic acid extract of cells on a support (such as nitrocellulose, nylon, polystyrene) and in

incubating, under well-defined conditions, the immobilized target nucleic acid with the probe. After hybridization, the excess of probe is eliminated and the hybrid molecules formed are detected by the appropriate method (measurement of the radioactivity, of the fluorescence or of the enzymatic activity linked to the probe).

5           The invention likewise comprises the nucleotide sequences according to the invention, characterized in that they are immobilized on a support, covalently or noncovalently.

          According to another advantageous mode of employing nucleotide sequences according to the invention, the latter can be used immobilized on a support and can  
10       thus serve to capture, by specific hybridization, the target nucleic acid obtained from the biological sample to be tested. If necessary, the solid support is separated from the sample and the hybridization complex formed between said capture probe and the target nucleic acid is then detected with the aid of a second probe, a so-called detection probe, labeled with an easily detectable element.

15           Another subject of the present invention is a vector for the cloning and/or expression of a sequence, characterized in that it contains a nucleotide sequence according to the invention.

          The vectors according to the invention, characterized in that they contain the elements allowing the expression and/or the secretion of said nucleotide sequences  
20       in a determined host cell, are likewise part of the invention.

          The vector must then contain a promoter, signals of initiation and termination of translation, as well as appropriate regions of regulation of transcription. It must be able to be maintained stably in the host cell and can optionally have particular signals specifying the secretion of the translated protein.  
25       These different elements are chosen as a function of the host cell used. To this end, the nucleotide sequences according to the invention can be inserted into autonomous replication vectors within the chosen host, or integrated vectors of the chosen host.

          Such vectors will be prepared according to the methods currently used by the person skilled in the art, and it will be possible to introduce the clones resulting

therefrom into an appropriate host by standard methods, such as, for example, lipofection, electroporation and thermal shock.

The vectors according to the invention are, for example, vectors of plasmid or viral origin.

5           A preferred vector for the expression of polypeptides of the invention is baculovirus.

The vector pBS KS in which is inserted the in-tandem DNA sequence of the PWD circovirus type A (or DFP) as deposited at the CNCM on 3 July 1997, under the number I-1891, is likewise preferred.

10           These vectors are useful for transforming host cells in order to clone or to express the nucleotide sequences of the invention.

The invention likewise comprises the host cells transformed by a vector according to the invention.

15           These cells can be obtained by the introduction into host cells of a nucleotide sequence inserted into a vector such as defined above, then the culturing of said cells under conditions allowing the replication and/or expression of the transfected nucleotide sequence.

20           The host cell can be selected from prokaryotic or eukaryotic systems, such as, for example, bacterial cells (Olins and Lee, 1993), but likewise yeast cells (Buckholz, 1993), as well as animal cells, in particular the cultures of mammalian cells (Edwards and Aruffo, 1993), and especially Chinese hamster ovary (CHO) cells, but likewise the cells of insects in which it is possible to use procedures employing baculoviruses, for example (Luckow, 1993).

25           A preferred host cell for the expression of the proteins of the invention is constituted by sf9 insect cells.

A more preferred host cell according to the invention is *E. coli*, such as deposited at the CNCM on 3 July 1997, under the number I-1891.

The invention likewise relates to animals comprising one of said transformed cells according to the invention.

The obtainment of transgenic animals according to the invention overexpressing one or more of the genes of PWD circovirus or part of the genes will be preferably carried out in rats, mice or rabbits according to methods well known to the person skilled in the art, such as by viral or nonviral transfections. It will be possible to obtain the transgenic animals overexpressing one or more of said genes by transfection of multiple copies of said genes under the control of a strong promoter of ubiquitous nature, or selective for one type of tissue. It will likewise be possible to obtain the transgenic animals by homologous recombination in embryonic cell strains, transfer of these cell strains to embryos, selection of the affected chimeras at the level of the reproductive lines, and growth of said chimeras.

The transformed cells as well as the transgenic animals according to the invention are utilizable in procedures for preparation of recombinant polypeptides.

It is today possible to produce recombinant polypeptides in relatively large quantity by genetic engineering using the cells transformed by expression vectors according to the invention or using transgenic animals according to the invention.

The procedures for preparation of a polypeptide of the invention in recombinant form, characterized in that they employ a vector and/or a cell transformed by a vector according to the invention and/or a transgenic animal comprising one of said transformed cells according to the invention, are themselves comprised in the present invention.

Among said procedures for preparation of a polypeptide of the invention in recombinant form, the preparation procedures employing a vector, and/or a cell transformed by said vector and/or a transgenic animal comprising one of said transformed cells, containing a nucleotide sequence according to the invention coding for a polypeptide of PWD circovirus, are preferred.

The recombinant polypeptides obtained as indicated above can just as well be present in glycosylated form as in nonglycosylated form and can or cannot have the natural tertiary structure.

A preferred variant consists in producing a recombinant polypeptide used to a "carrier" protein (chimeric protein). The advantage of this system is that it allows a stabilization of and a decrease in the proteolysis of the recombinant product, an increase in the solubility in the course of renaturation in vitro and/or a simplification of the purification when the fusion partner has an affinity for a specific ligand.

More particularly, the invention relates to a procedure for preparation of a polypeptide of the invention comprising the following steps:

- a) culture of transformed cells under conditions allowing the expression of a recombinant polypeptide of nucleotide sequence according to the invention;
- b) if need be, recovery of said recombinant polypeptide.

When the procedure for preparation of a polypeptide of the invention employs a transgenic animal according to the invention, the recombinant polypeptide is then extracted from said animal.

The invention also relates to a polypeptide which is capable of being obtained by a procedure of the invention such as described previously.

The invention also comprises a procedure for preparation of a synthetic polypeptide, characterized in that it uses a sequence of amino acids of polypeptides according to the invention.

The invention likewise relates to a synthetic polypeptide obtained by a procedure according to the invention.

The polypeptides according to the invention can likewise be prepared by techniques which are conventional in the field of the synthesis of peptides. This synthesis can be carried out in homogeneous solution or in solid phase.

For example, recourse can be made to the technique of synthesis in homogeneous solution described by Houben-Weyl in 1974.

This method of synthesis consists in successively condensing, two by two, the successive amino acids in the order required, or in condensing amino acids and fragments formed previously and already containing several amino acids in the appropriate order, or alternatively several fragments previously prepared in this

way, it being understood that it will be necessary to protect beforehand all the reactive functions carried by these amino acids or fragments, with the exception of amine functions of one and carboxyls of the other or vice-versa, which must normally be involved in the formation of peptide bonds, especially after activation of the carboxyl function, according to the methods well known in the synthesis of peptides.

According to another preferred technique of the invention, recourse will be made to the technique described by Merrifield.

To make a peptide chain according to the Merrifield procedure, recourse is made to a very porous polymeric resin, on which is immobilized the first C-terminal amino acid of the chain. This amino acid is immobilized on a resin through its carboxyl group and its amine function is protected. The amino acids which are going to form the peptide chain are thus immobilized, one after the other, on the amino group, which is deprotected beforehand each time, of the portion of the peptide chain already formed; and which is attached to the resin. When the whole of the desired peptide chain has been formed, the protective groups of the different amino acids forming the peptide chain are eliminated and the peptide is detached from the resin with the aid of an acid.

The invention additionally relates to hybrid polypeptides having at least one polypeptide according to the invention, and a sequence of a polypeptide capable of inducing an immune response in man or animals.

Advantageously, the antigenic determinant is such that it is capable of inducing a humoral and/or cellular response.

It will be possible for such a determinant to comprise a polypeptide according to the invention in glycosylated form used with a view to obtaining immunogenic compositions capable of inducing the synthesis of antibodies directed against multiple epitopes. Said polypeptides or their glycosylated fragments are likewise part of the invention.



5       These hybrid molecules can be formed, in part, of a polypeptide carrier molecule or of fragments thereof according to the invention, associated with a possibly immunogenic part, in particular an epitope of the diphtheria toxin, the tetanus toxin, a surface antigen of the hepatitis B virus (patent FR 79 21811), the VP1 antigen of the poliomyelitis virus or any other viral or bacterial toxin or antigen.

10       The procedures for synthesis of hybrid molecules encompass the methods used in genetic engineering for constructing hybrid nucleotide sequences coding for the polypeptide sequences sought. It will be possible, for example, to refer advantageously to the technique for obtainment of genes coding for fusion proteins described by Minton in 1984.

15       Said hybrid nucleotide sequences coding for a hybrid polypeptide as well as the hybrid polypeptides according to the invention characterized in that they are recombinant polypeptides obtained by the expression of said hybrid nucleotide sequences are likewise part of the invention.

20       The invention likewise comprises the vectors characterized in that they contain one of said hybrid nucleotide sequences. The host cells transformed by said vectors, the transgenic animals comprising one of said transformed cells as well as the procedures for preparation of recombinant polypeptides using said vectors, said transformed cells and/or said transgenic animals are, of course, likewise part of the invention.

25       The polypeptides according to the invention, the antibodies according to the invention described below and the nucleotide sequences according to the invention can advantageously be employed in procedures for the detection and/or identification of PWD circovirus, or of porcine circovirus other than a PWD circovirus, in a biological sample (biological tissue or fluid) capable of containing them. These procedures, according to the specificity of the polypeptides, the antibodies and the nucleotide sequences according to the invention which will be used, will in particular be able to detect and/or to identify a PWD circovirus or a

porcine circovirus other than a PWD circovirus or other than the PWD circovirus of type B.

The polypeptides according to the invention can advantageously be employed in a procedure for the detection and/or the identification of PWD circovirus of type A, of type B, of type A or B, or porcine circovirus other than the PWD circovirus of type B, or of porcine circovirus other than the PWD circovirus of type A or B, in a biological sample (biological tissue or fluid) capable of containing them, characterized in that it comprises the following steps:

- a) contacting of this biological sample with a polypeptide or one of its fragments according to the invention (under conditions allowing an immunological reaction between said polypeptide and the antibodies possibly present in the biological sample);
- b) demonstration of the antigen-antibody complexes possibly formed.

In the present description, PWD circovirus, except if a particular mention is indicated, will be understood as designating a PWD circovirus of type A or of type B, and porcine circovirus other than PWD, except if a particular mention is indicated, will be understood as designating a porcine circovirus other than a PWD circovirus of type A and B.

Preferably, the biological sample is formed by a fluid, for example a pig serum, whole blood or biopsies.

Any conventional procedure can be employed for carrying out such a detection of the antigen-antibody complexes possibly formed.

By way of example, a preferred method brings into play immunoenzymatic processes according to the ELISA technique, by immunofluorescence, or radioimmunological processes (RIA) or their equivalent.

Thus, the invention likewise relates to the polypeptides according to the invention, labeled with the aid of an adequate label such as of the enzymatic, fluorescent or radioactive type.

Such methods comprise, for example, the following steps:

- deposition of determined quantities of a polypeptide composition according to the invention in the wells of a microtiter plate,
- introduction into said wells of increasing dilutions of serum, or of a biological sample other than that defined previously, having to be analyzed,
- 5       - incubation of the microplate,
- introduction into the wells of the microtiter plate of labeled antibodies directed against pig immunoglobulins, the labeling of these antibodies having been carried out with the aid of an enzyme selected from those which are capable of hydrolyzing a substrate by modifying the absorption of the radiation of the latter, at least at a determined wavelength, for example at 10       550 nm,
- detection, by comparison with a control test, of the quantity of hydrolyzed substrate.

The invention likewise relates to a kit or set for the detection and/or 15 identification of PWD circovirus, of porcine circovirus other than a PWD circovirus or of porcine circovirus other than the PWD circovirus of type B, characterized in that it comprises the following elements:

- a polypeptide according to the invention,
- if need be, the reagents for the formation of the medium favorable to the immunological or specific reaction,
- 20       - if need be, the reagents allowing the detection of the antigen-antibody complexes produced by the immunological reaction between the polypeptide(s) of the invention and the antibodies possibly present in the biological sample, these reagents likewise being able to carry a label, or to be recognized in their turn by a labeled reagent, more particularly in the case 25       where the polypeptide according to the invention is not labeled,
- if need be, a biological reference sample (negative control) devoid of antibodies recognized by a polypeptide according to the invention,

- if need be, a biological reference sample (positive control) containing a predetermined quantity of antibodies recognized by a polypeptide according to the invention.

5 The polypeptides according to the invention allow monoclonal or polyclonal antibodies to be prepared which are characterized in that they specifically recognize the polypeptides according to the invention. It will advantageously be possible to prepare the monoclonal antibodies from hybridomas according to the technique described by Kohler and Milstein in 1975. It will be possible to prepare the polyclonal antibodies, for example, by immunization of an animal, in particular 10 mouse, with a polypeptide or a DNA, according to the invention, associated with an adjuvant of the immune response, and then purification of the specific antibodies contained in the serum of the immunized animals on an affinity column on which the polypeptide which has served as an antigen has previously been immobilized. The polyclonal antibodies according to the invention can also be prepared by 15 purification, on an affinity column on which a polypeptide according to the invention has previously been immobilized, of the antibodies contained in the serum of pigs infected by a PWD circovirus.

The invention likewise relates to mono- or polyclonal antibodies or their fragments, or chimeric antibodies, characterized in that they are capable of 20 specifically recognizing a polypeptide according to the invention.

It will likewise be possible for the antibodies of the invention to be labeled in the same manner as described previously for the nucleic probes of the invention, such as a labeling of enzymatic, fluorescent or radioactive type.

25 The invention is additionally directed at a procedure for the detection and/or identification of PWD circovirus, of porcine circovirus other than a PWD circovirus, or other than the PWD circovirus of type B, in a biological sample, characterized in that it comprises the following steps:

a) contacting of the biological sample (biological tissue or fluid) with a mono- or polyclonal antibody according to the invention (under conditions allowing

an immunological reaction between said antibodies and the polypeptides of PWD circovirus, of porcine circovirus other than a PWD circovirus, of porcine circovirus other than the PWD circovirus of type B, possibly present in the biological sample);

b) demonstration of the antigen-antibody complex possibly formed.

5 Likewise within the scope of the invention is a kit or set for the detection and/or the identification of PWD circovirus, of porcine circovirus other than a PWD circovirus or of porcine circovirus other than the PWD circovirus of type B, characterized in that it comprises the following components:

- 10 - a polyclonal or monoclonal antibody according to the invention, if need be labeled;
- if need be, a reagent for the formation of the medium favorable to the carrying out of the immunological reaction;
- if need be, a reagent allowing the detection of the antigen-antibody complexes produced by the immunological reaction, this reagent likewise  
15 being able to carry a label, or being capable of being recognized in its turn by a labeled reagent, more particularly in the case where said monoclonal or polyclonal antibody is not labeled;
- if need be, reagents for carrying out the lysis of cells of the sample tested.

20 The present invention likewise relates to a procedure for the detection and/or the identification of PWD, of porcine circovirus other than a PWD circovirus or of porcine circovirus other than the PWD circovirus of type B, in a biological sample, characterized in that it employs a nucleotide sequence according to the invention.

25 More particularly, the invention relates to a procedure for the detection and/or the identification of PWD circovirus, of porcine circovirus other than a PWD circovirus or of porcine circovirus other than the PWD circovirus of type B, in a biological sample, characterized in that it contains the following steps:

a) if need be, isolation of the DNA from the biological sample to be analyzed;

- b) specific amplification of the DNA of the sample with the aid of at least one primer, or a pair of primers, according to the invention;
- c) demonstration of the amplification products.

5 These can be detected, for example, by the technique of molecular hybridization utilizing a nucleic probe according to the invention. This probe will advantageously be labeled with a nonradioactive (cold probe) or radioactive element.

10 For the purposes of the present invention, "DNA of the biological sample" or "DNA contained in the biological sample" will be understood as meaning either the DNA present in the biological sample considered, or possibly the cDNA obtained after the action of an enzyme of reverse transcriptase type on the RNA present in said biological sample.

Another aim of the present invention consists in a procedure according to the invention, characterized in that it comprises the following steps:

- 15 a) contacting of a nucleotide probe according to the invention with a biological sample, the DNA contained in the biological sample having, if need be, previously been made accessible to hybridization under conditions allowing the hybridization of the probe with the DNA of the sample;
- b) demonstration of the hybrid formed between the nucleotide probe and  
20 the DNA of the biological sample.

The present invention also relates to a procedure according to the invention, characterized in that it comprises the following steps:

- 25 a) contacting of a nucleotide probe immobilized on a support according to the invention with a biological sample, the DNA of the sample having, if need be, previously been made accessible to hybridization, under conditions allowing the hybridization of the probe with the DNA of the sample;
- b) contacting of the hybrid formed between the nucleotide probe immobilized on a support and the DNA contained in the biological sample, if need

be after elimination of the DNA of the biological sample which has not hybridized with the probe; with a nucleotide probe labeled according to the invention;

c) demonstration of the novel hybrid formed in step b).

5 According to an advantageous embodiment of the procedure for detection and/or identification defined previously, this is characterized in that, prior to step a), the DNA of the biological sample is first amplified with the aid of at least one primer according to the invention.

10 The invention is additionally directed at a kit or set for the detection and/or the identification of PWD circovirus, of porcine circovirus other than the PWD circovirus or of porcine circovirus other than the PWD circovirus of type B, characterized in that it comprises the following elements:

a) a nucleotide probe according to the invention;

b) if need be, the reagents necessary for the carrying out of a hybridization reaction;

15 c) if need be, at least one primer according to the invention as well as the reagents necessary for an amplification reaction of the DNA.

20 The invention likewise relates to a kit or set for the detection and/or the identification of PWD circovirus, of porcine circovirus other than a PWD circovirus or of porcine circovirus other than the PWD circovirus of type B, characterized in that it comprises the following components:

a) a nucleotide probe, called a capture probe, according to the invention;

b) an oligonucleotide probe, called a revealing probe, according to the invention,

25 c) if need be, at least one primer according to the invention, as well as the reagents necessary for an amplification reaction of the DNA.

The invention also relates to a kit or set for the detection and/or identification of PWD circovirus, of porcine circovirus other than a PWD circovirus

or of porcine circovirus other than the PWD circovirus of type B, characterized in that it comprises the following elements:

- a) at least one primer according to the invention;
- b) if need be, the reagents necessary for carrying out a DNA  
5 amplification reaction;
- c) if need be, a component allowing the sequence of the amplified fragment to be verified, more particularly an oligonucleotide probe according to the invention.

The invention additionally relates to the use of a nucleotide sequence  
10 according to the invention, of a polypeptide according to the invention, of an antibody according to the invention, of a cell according to the invention, and/or of an animal transformed according to the invention, for the selection of an organic or inorganic compound capable of modulating, inducing or inhibiting the expression of genes, and/or of modifying the cellular replication of PWD circovirus or capable of  
15 inducing or of inhibiting the pathologies linked to an infection by a PWD circovirus.

The invention likewise comprises a method of selection of compounds capable of binding to a polypeptide or one of its fragments according to the invention, capable of binding to a nucleotide sequence according to the invention, or capable of recognizing an antibody according to the invention, and/or capable of  
20 modulating, inducing or inhibiting the expression of genes, and/or of modifying the cellular replication of PWD circovirus or capable of inducing or inhibiting the pathologies linked to an infection by a PWD circovirus, characterized in that it comprises the following steps:

- a) contacting of said compound with said polypeptide, said nucleotide  
25 sequence, or with a cell transformed according to the invention and/or administration of said compound to an animal transformed according to the invention;
- b) determination of the capacity of said compound to bind to said polypeptide or said nucleotide sequence, or to modulate, induce or inhibit the



expression of genes, or to modulate the growth or the replication of PWD circovirus, or to induce or inhibit in said transformed animal the pathologies linked to an infection by PWD circovirus (designated activity of said compound).

5 The compounds capable of being selected can be organic compounds such as polypeptides or carbohydrates or any other organic or inorganic compounds already known, or novel organic compounds elaborated by molecular modelling techniques and obtained by chemical or biochemical synthesis, these techniques being known to the person skilled in the art.

10 It will be possible to use said selected compounds to modulate the cellular replication of PWD circovirus and thus to control infection by this virus, the methods allowing said modulations to be determined being well known to the person skilled in the art.

15 This modulation can be carried out, for example, by an agent capable of binding to a protein and thus of inhibiting or of potentiating its biological activity, or capable of binding to an envelope protein of the external surface of said virus and of blocking the penetration of said virus into the host cell or of favoring the action of the immune system of the infected organism directed against said virus. This modulation can likewise be carried out by an agent capable of binding to a nucleotide sequence of a DNA of said virus and of blocking, for example, the  
20 expression of a polypeptide whose biological or structural activity is necessary for the replication or for the proliferation of said virus host cells to host cells in the host animal.

The invention relates to the compounds capable of being selected by a selection method according to the invention.

25 The invention likewise relates to a pharmaceutical composition comprising a compound selected from the following compounds:

- a) a nucleotide sequence according to the invention;
- b) a polypeptide according to the invention;

c) a vector, a viral particle or a cell transformed according to the invention;

d) an antibody according to the invention;

5 e) a compound capable of being selected by a selection method according to the invention;

possibly in combination with a pharmaceutically acceptable vehicle and, if need be, with one or more adjuvants of the appropriate immunity.

10 The invention also relates to an immunogenic and/or vaccine composition, characterized in that it comprises a compound selected from the following compounds:

a) a nucleotide sequence according to the invention;

b) a polypeptide according to the invention;

c) a vector or a viral particle according to the invention; and

d) a cell according to the invention.

15 In one embodiment, the vaccine composition according to the invention is characterized in that it comprises a mixture of at least two of said compounds a), b), c) and d) above and in that one of the two said compounds is related to the PWD circovirus of type A and the other is related to the PWD circovirus of type B.

20 In another embodiment of the invention, the vaccine composition is characterized in that it comprises at least one compound a), b), c), or d) above which is related to PWD circovirus of type B. In still another embodiment, the vaccine composition is characterized in that it comprises at least one compound a), b), c), or d) above which is related to PWD circovirus of type B ORF'2.

25 A compound related to the PWD circovirus of type A or of type B is understood here as respectively designating a compound obtained from the genomic sequence of the PWD circovirus of type A or of type B.

The invention is additionally aimed at an immunogenic and/or vaccine composition, characterized in that it comprises at least one of the following compounds:

- a nucleotide sequence SEQ ID No. 23, SEQ ID No. 25, or one of their fragments or homologues;
- a polypeptide of sequence SEQ ID No. 24, SEQ ID No. 26, or one of their fragments, or a modification thereof;
- 5       - a vector or a viral particle comprising a nucleotide sequence SEQ ID No. 23, SEQ ID No. 25, or one of their fragments or homologues;
- a transformed cell capable of expressing a polypeptide of sequence SEQ ID No. 24, SEQ ID No. 26, or one of their fragments, or a modification thereof; or
- 10       - a mixture of at least two of said compounds.

The invention also comprises an immunogenic and/or vaccine composition according to the invention, characterized in that it comprises said mixture of at least two of said compounds as a combination product for simultaneous, separate or protracted use for the prevention or the treatment of infection by a PWD circovirus, especially of type B.

In a preferred embodiment, the vaccine composition according to the invention comprises the mixture of the following compounds:

- a pcDNA3 plasmid containing a nucleic acid of sequence SEQ ID No. 23;
- a pcDNA3 plasmid containing a nucleic acid of sequence SEQ ID No. 25;
- 20       - a pcDNA3 plasmid containing a nucleic acid coding for the GM-CSF protein;
- a recombinant baculovirus containing a nucleic acid of sequence SEQ ID No. 23;
- a recombinant baculovirus containing a nucleic acid of sequence SEQ ID No. 25; and
- 25       - if need be, an adjuvant of the appropriate immunity, especially the adjuvant AIF<sup>TM</sup>.

The invention is likewise directed at a pharmaceutical composition according to the invention, for the prevention or the treatment of an infection by a PWD circovirus.

5 The invention is also directed at a pharmaceutical composition according to the invention for the prevention or the treatment of an infection by the PWD circovirus of type B.

10 The invention likewise concerns the use of a composition according to the invention, for the preparation of a medicament intended for the prevention or the treatment of infection by a PWD circovirus, preferably by the PWD circovirus of type B.

Under another aspect, the invention relates to a vector, a viral particle or a cell according to the invention, for the treatment and/or the prevention of a disease by gene therapy.

15 Finally, the invention comprises the use of a vector, of a viral particle or of a cell according to the invention for the preparation of a medicament intended for the treatment and/or the prevention of a disease by gene therapy.

20 The polypeptides of the invention entering into the immunogenic or vaccine compositions according to the invention can be selected by techniques known to the person skilled in the art such as, for example, depending on the capacity of said polypeptides to stimulate the T cells, which is translated, for example, by their proliferation or the secretion of interleukins, and which leads to the production of antibodies directed against said polypeptides.

25 In pigs, as in mice, in which a weight dose of the vaccine composition comparable to the dose used in man is administered, the antibody reaction is tested by taking of the serum followed by a study of the formation of a complex between the antibodies present in the serum and the antigen of the vaccine composition, according to the usual techniques.

The pharmaceutical compositions according to the invention will contain an effective quantity of the compounds of the invention, that is to say in sufficient

quantity of said compound(s) allowing the desired effect to be obtained, such as, for example, the modulation of the cellular replication of PWD circovirus. The person skilled in the art will know how to determine this quantity, as a function, for example, of the age and of the weight of the individual to be treated, of the state of advancement of the pathology, of the possible secondary effects and by means of a test of evaluation of the effects obtained on a population range, these tests being known in these fields of application.

According to the invention, said vaccine combinations will preferably be combined with a pharmaceutically acceptable vehicle and, if need be, with one or more adjuvants of the appropriate immunity.

Today, various types of vaccines are available for protecting animals or man against infectious diseases: attenuated living microorganisms (*M. bovis* - BCG for tuberculosis), inactivated microorganisms (influenza virus), acellular extracts (*Bordetella pertussis* for whooping cough), recombined proteins (surface antigen of the hepatitis B virus), polysaccharides (pneumococcal). Vaccines prepared from synthetic peptides or genetically modified microorganisms expressing heterologous antigens are in the course of experimentation. More recently still, recombined plasmid DNAs carrying genes coding for protective antigens have been proposed as an alternative vaccine strategy. This type of vaccination is carried out with a particular plasmid originating from a plasmid of *E.coli* which does not replicate *in vivo* and which codes uniquely for the vaccinating protein. Animals have been immunized by simply injecting the naked plasmid DNA into the muscle. This technique leads to the expression of the vaccine protein *in situ* and to an immune response of cellular type (CTL) and of humoral type (antibody). This double induction of the immune response is one of the principal advantages of the vaccination technique with naked DNA.

The vaccine compositions comprising nucleotide sequences or vectors into which are inserted said sequences are especially described in the international

application No. WO 90/11092 and likewise in the international application No. WO 95/11307.

5 The constitutive nucleotide sequence of the vaccine composition according to the invention can be injected into the host after having been coupled to compounds which favor the penetration of this polynucleotide into the interior of the cell or its transport to the cell nucleus. The resultant conjugates can be encapsulated in polymeric microparticles, as described in the international application No. WO 94/27238 (Medisorb Technologies International).

10 According to another embodiment of the vaccine composition according to the invention, the nucleotide sequence, preferably a DNA, is complexed with DEAE-dextran (Pagano et al., 1967) or with nuclear proteins (Kaneda et al., 1989), with lipids (Felgner et al., 1987) or encapsulated in liposomes (Fraley et al., 1980) or else introduced in the form of a gel facilitating its transfection into the cells (Midoux et al., 1993, Pastore et al., 1994). The polynucleotide or the vector  
15 according to the invention can also be in suspension in a buffer solution or be combined with liposomes.

Advantageously, such a vaccine will be prepared according to the technique described by Tacson et al. or Huygen et al. in 1996 or alternatively according to the technique described by Davis et al. in the international application No. WO  
20 95/11307.

Such a vaccine can likewise be prepared in the form of a composition containing a vector according to the invention, placed under the control of regulation elements allowing its expression in man or animal. It will be possible, for example, to use, by way of *in vivo* expression vector of the polypeptide antigen of  
25 interest, the plasmid pcDNA3 or the plasmid pcDNA1/neo, both marketed by Invitrogen (R&D Systems, Abingdon, United Kingdom). It is also possible to use the plasmid V1Jns.tPA, described by Shiver et al. in 1995. Such a vaccine will advantageously comprise, apart from the recombinant vector, a saline solution, for example a sodium chloride solution.

Pharmaceutically acceptable vehicle is understood as designating a compound or a combination of compounds entering into a pharmaceutical composition or vaccine which does not provoke secondary reactions and which allows, for example, the facilitation of the administration of the active compound, an increase in its duration of life and/or its efficacy in the body, an increase in its solubility in solution or alternatively an improvement in its conservation. These pharmaceutically acceptable vehicles are well known and will be adapted by the person skilled in the art as a function of the nature and of the mode of administration of the chosen active compound.

As far as the vaccine formulations are concerned, these can comprise adjuvants of the appropriate immunity which are known to the person skilled in the art, such as, for example, aluminum hydroxide, a representative of the family of muramyl peptides such as one of the peptide derivatives of N-acetyl muramyl, a bacterial lysate, or alternatively Freund's incomplete adjuvant.

These compounds can be administered by the systemic route, in particular by the intravenous route, by the intramuscular, intradermal or subcutaneous route, or by the oral route. In a more preferred manner, the vaccine composition comprising polypeptides according to the invention will be administered by the intramuscular route, through the food or by nebulization several times, staggered over time.

Their administration modes, dosages and optimum pharmaceutical forms can be determined according to the criteria generally taken into account in the establishment of a treatment adapted to an animal such as, for example, the age or the weight, the seriousness of its general condition, the tolerance to the treatment and the secondary effects noted. Preferably, the vaccine of the present invention is administered in an amount that is protective against piglet weight loss disease.

For example, in the case of a vaccine according to the present invention comprising a polypeptide encoded by a nucleotide sequence of the genome of PCV, or a homologue or fragment thereof, the polypeptide will be administered one time or several times, spread out over time, directly or by means of a transformed cell

capable of expressing the polypeptide, in an amount of about 0.1 to 10  $\mu\text{g}$  per kilogram weight of the animal, preferably about 0.2 to about 5  $\mu\text{g}/\text{kg}$ , more preferably about 0.5 to about 2  $\mu\text{g}/\text{kg}$  for a dose.

5 The present invention likewise relates to the use of nucleotide sequences of PWD circovirus according to the invention for the construction of autoreplicative retroviral vectors and the therapeutic applications of these, especially in the field of human gene therapy in vivo.

10 The feasibility of gene therapy applied to man no longer needs to be demonstrated and this relates to numerous therapeutic applications like genetic diseases, infectious diseases and cancers. Numerous documents of the prior art describe the means of employing gene therapy, especially through viral vectors. Generally speaking, the vectors are obtained by deletion of at least some of the viral genes which are replaced by the genes of therapeutic interest. Such vectors can be propagated in a complementation line which supplies in trans the deleted viral  
15 functions in order to generate a defective viral vector particle for replication but capable of infecting a host cell. To date, the retroviral vectors are amongst the most widely used and their mode of infection is widely described in the literature accessible to the person skilled in the art.

20 The principle of gene therapy is to deliver a functional gene, called a gene of interest, of which the RNA or the corresponding protein will produce the desired biochemical effect in the targeted cells or tissues. On the one hand, the insertion of genes allows the prolonged expression of complex and unstable molecules such as RNAs or proteins which can be extremely difficult or even impossible to obtain or to administer directly. On the other hand, the controlled insertion of the desired  
25 gene into the interior of targeted specific cells allows the expression product to be regulated in defined tissues. For this, it is necessary to be able to insert the desired therapeutic gene into the interior of chosen cells and thus to have available a method of insertion capable of specifically targeting the cells or the tissues chosen.



Among the methods of insertion of genes, such as, for example, microinjection, especially the injection of naked plasmid DNA (Derse, D. et al., 1995, and Zhao, T.M. et al., 1996), electroporation, homologous recombination, the use of viral particles, such as retroviruses, is widespread. However, applied in vivo, the gene transfer systems of recombinant retroviral type at the same time have a weak infectious power (insufficient concentration of viral particles) and a lack of specificity with regard to chosen target cells.

The production of cell-specific viral vectors, having a tissue-specific tropism, and whose gene of interest can be translated adequately by the target cells, is realizable, for example, by fusing a specific ligand of the target host cells to the N-terminal part of a surface protein of the envelope of PWD circovirus. It is possible to mention, for example, the construction of retroviral particles having the CD4 molecule on the surface of the envelope so as to target the human cells infected by the HIV virus (YOUNG, J.A.T. et al., Sciences 1990, 250, 1421-1423), viral particles having a peptide hormone fused to an envelope protein to specifically infect the cells expressing the corresponding receptor (KASAHARA, N. et al., Sciences 1994, 266, 1373-1376) or else alternatively viral particles having a fused polypeptide capable of immobilizing on the receptor of the epidermal growth factor (EGF) (COSSET, F.L. et al., J. of Virology 1995, 69, 10, 6314-6322). In another approach, single-chain fragments of antibodies directed against surface antigens of the target cells are inserted by fusion with the N-terminal part of the envelope protein (VALSESIA-WITTMAN, S. et al., J. of Virology 1996, 70, 3, 2059-2064; TEARINA CHU, T.H. et al., J. of Virology 1997, 71, 1, 720-725).

For the purposes of the present invention, a gene of interest in use in the invention can be obtained from a eukaryotic or prokaryotic organism or from a virus by any conventional technique. It is, preferably, capable of producing an expression product having a therapeutic effect and it can be a product homologous to the cell host or, alternatively, heterologous. In the scope of the present invention, a gene of interest can code for an (i) intracellular or (ii) membrane product present on the

surface of the host cell or (iii) secreted outside the host cell. It can therefore comprise appropriate additional elements such as, for example, a sequence coding for a secretion signal. These signals are known to the person skilled in the art.

5 In accordance with the aims pursued by the present invention, a gene of interest can code for a protein corresponding to all or part of a native protein as found in nature. It can likewise be a chimeric protein, for example arising from the fusion of polypeptides of various origins or from a mutant having improved and/or modified biological properties. Such a mutant can be obtained, by conventional biological techniques, by substitution, deletion and/or addition of one or more  
10 amino acid residues.

It is very particularly preferred to employ a gene of therapeutic interest coding for an expression product capable of inhibiting or retarding the establishment and/or the development of a genetic or acquired disease. A vector according to the invention is in particular intended for the prevention or for the treatment of cystic  
15 fibrosis, of hemophilia A or B, of Duchenne's or Becker's myopathy, of cancer, of AIDS and of other bacteria or infectious diseases due to a pathogenic organism: virus, bacteria, parasite or prion. The genes of interest utilizable in the present invention are those which code, for example, for the following proteins:

- a cytokine and especially an interleukin, an interferon, a tissue necrosis  
20 factor and a growth factor and especially a hematopoietic growth factor (G-CSF, GM-CSF),
- a factor or cofactor involved in clotting and especially factor VIII, von Willebrand's factor, antithrombin III, protein C, thrombin and hirudin,
- an enzyme or an enzyme inhibitor such as the inhibitors of viral proteases,
- 25 - an expression product of a suicide gene such as thymidine kinase of the HSV virus (herpesvirus) of type 1,
- an activator or an inhibitor of ion channels,
- a protein of which the absence, the modification or the deregulation of expression is responsible for a genetic disease, such as the CFTR protein,

dystrophin or minidystrophin, insulin, ADA (adenosine diaminase), glucocerebrosidase and phenylhydroxylase,

- a protein capable of inhibiting the initiation or the progression of cancers, such as the expression products of tumor suppressor genes, for example the P53 and Rb genes,
- a protein capable of stimulating an immune or an antibody response, and
- a protein capable of inhibiting a viral infection or its development, for example the antigenic epitopes of the virus in question or altered variants of viral proteins capable of entering into competition with the native viral proteins.

The invention thus relates to the vectors characterized in that they comprise a nucleotide sequence of PWD circovirus according to the invention, and in that they additionally comprise a gene of interest.

The present invention likewise relates to viral particles generated from said vector according to the invention. It additionally relates to methods for the preparation of viral particles according to the invention, characterized in that they employ a vector according to the invention, including viral pseudoparticles (VLP, virus-like particles).

The invention likewise relates to animal cells transfected by a vector according to the invention.

Likewise comprised in the invention are animal cells, especially mammalian, infected by a viral particle according to the invention.

The present invention likewise relates to a vector, a viral particle or a cell according to the invention, for the treatment and/or the prevention of a genetic disease or of an acquired disease such as cancer or an infectious disease. The invention is likewise directed at a pharmaceutical composition comprising, by way of therapeutic or prophylactic agent, a vector or a cell according to the invention, in combination with a vehicle acceptable from a pharmaceutical point of view.

Other characteristics and advantages of the invention appear in the examples and the figures.

The invention is described in more detail in the following illustrative examples. Although the examples may represent only selected embodiments of the invention, it should be understood that the following examples are illustrative and not limiting.

### Examples

#### EXAMPLE 1: Cloning, sequencing and characterization of the PWD circovirus of type A (PCVA)

##### 1. Experimental procedures

Experimental reproduction of the infection and its syndrome (cf. Figure 1).

A first test was carried out with pigs from a very well-kept farm, but affected by piglet weight loss disease (PWD), likewise called fatal piglet wasting (FPW). Tests carried out with SPF (specific pathogen-free) pigs showed a transfer of contaminant(s) finding expression in a complex pathology combining hyperthermia, retardation of growth, diarrhea and conjunctivitis. The PDRS (porcine dysgenic and respiratory syndrome) virus, an infectious disease due to an arteriovirus) was rapidly isolated from breeding pigs and contact pigs. It should have been possible to attribute all the clinical signs to the presence of the PDRS virus. However, two farm pigs presented signs of FPW without the PDRS virus being isolated. The histological analyses and blood formulas, however, showed that these pigs were suffering from an infectious process of viral origin.

In a second test, 8-week SPF pigs were inoculated by the intratracheal route with organ homogenates of two farm pigs suffering from FPW. The inoculated pigs exhibited hyperthermia 8 to 9 days post-infection, then their growth was retarded. Other SPF pigs, placed in contact, had similar, attenuated signs 30 days after the

initial experiment. No seroconversion with respect to a European or Canadian strain of PDRS virus was recorded in these animals.

A third test allowed the syndrome to be reproduced from samples taken from the pigs of the second test.

5

### Conclusion

The syndrome is reproduced under the experimental conditions. It is determined by at least one infectious agent, which is transmittable by direct contact. The clinical constants are a sometimes high hyperthermia (greater than or equal to 41.5°C) which develops 8 to 10 days after infection. Retardation of the growth can be observed. The other signs are a reversal of the blood formula (reversal of the lymphocyte/polynuclear ratio from 70/30 to 30/70) and frequent lesions on the ganglia, especially those draining the respiratory apparatus (ganglionic hypertrophy, loss of structure with necrosis and infiltration by mononucleated or plurinucleated giant cells).

15

### 2. Laboratory studies

Various cell supports including primary pig kidney cells or cell lines, pig testicle cells, monkey kidney cells, pig lymphocytes, pig alveolar macrophages and circulating blood monocytes were used to demonstrate the possible presence of a virus. No cytopathic effect was demonstrated in these cells. On the other hand, the use of a serum of a pig sick after experimental infection allowed an intracellular antigen to be revealed in the monocytes, the macrophages and approximately 10% of pig kidney (PK) cells infected with organ homogenates. This indirect revealing was carried out kinetically at different culture times. It is evident from this that the antigen initially appears in the nucleus of the infected cells before spreading into the cytoplasm. The successive passages in cell culture did not allow the signal to be amplified.

25

Under electron-microscopy on organ homogenates, spherical particles labeled specifically by the serum of sick pigs, infected under the experimental conditions, were visualized. The size of these particles is estimated at 20 nm.

After two passages of these organ homogenates over pig lymphocytes and then three passages over pig kidney or testicle cells, a cytopathic effect developed and was amplified. An adenovirus was visualized in the electron microscope, which, under the experimental conditions, did not reproduce FPW (only a hyperthermia peak was noted 24 to 48 hours after infection, and then nothing more).

It has been possible to demonstrate DNA bands in certain samples of pigs infected under the experimental conditions and having exhibited signs of the disease (results not shown). A certain connection exists between the samples giving a positive result in cell culture and those having a DNA band.

### Conclusion

At least two types of virus were demonstrated in the organ homogenates from pigs suffering from FPW. One is an adenovirus, but by itself alone it does not reproduce the disease. The other type of virus is a circovirus and is associated with FPW. This circovirus, of which two types have been isolated and sequenced, designated below PWD circovirus type A (or PCVA) and PWD circovirus of type B (or PCVB) have mutations with respect to the known sequences of circovirus which are nonpathogenic for the pig.

### 3. Cloning and sequencing of the DNA of the PWD circovirus of type A

Extraction of the replicative form (RF) DNA, cleavage by the Kpn I enzyme and amplification by a pair of primers flanking the Kpn I restriction site. Sequencing of the two strands at least twice by the Sanger method.

The nucleic sequence of the strand of (+) polarity of the genome of the PWD circovirus of type A (or PCVA), strain FPW, is represented by the sequence SEQ ID No. 1 in the list of sequences, the nucleic sequence of the strand of (-) polarity of the genome of the PWD circovirus of type A (or PCVA) being represented by the nucleic sequence 3' → 5' of Figure 3 or by the sequence SEQ ID No. 5 (represented according to the orientation 5' → 3') in the list of sequences.

The amino acid sequences SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14 of the list of sequences respectively represent the sequences of proteins

encoded by the nucleic sequences of the 3 open reading frames SEQ ID No. 9 (ORF1); corresponding to the REP protein, SEQ ID No. 11 (ORF2) and SEQ ID No. 13 (ORF3), determined from the sequence SEQ ID No. 1 of the strand of (+) polarity or of the nucleic sequence SEQ ID No. 5 of the strand of (-) polarity of the genome of the PWD circovirus of type A.

4. Comparison of the nucleotide sequences and amino acids of the PWD circovirus of type A (or associated with PWD) which are obtained with the corresponding sequences of MEEHAN and MANKERTZ circoviruses of porcine cell lines

Use of the DNA sequence analysis software, DNASIS.

Sequences of oligonucleotides used as primers or probes in the detection and/or identification procedures

1. Specific detection of the PWD circovirus of type A:

SEQ ID No. 46      primer PCV 5: 5' GTG TGC TCG ACA TTG GTG TG 3';

SEQ ID No. 47      primer PCV 10: 5' TGG AAT GTT AAC GAG CTG AG 3';

2. Specific detection of the circovirus of the cell lines:

SEQ ID No. 46      primer PCF 5: 5' GTG TGC TCG ACA TTG GTG TG 3';

SEQ ID No. 52      primer MEE 1: 5' TGG AAT GTT AAC TAC CTC AA 3';

3. Differential detection:

the pairs of primers used are those described, for example, in the paragraphs 1 and 2 above;

4. Detection of the monomeric circular replicative forms RF:

SEQ ID No. 46      primer PCV 5: 5' GTG TGC TCG ACA TTG GTG TG 3';

SEQ ID No. 48      primer PCV 6: 5' CTC GCA GCC ATC TTG GAA TG 3';

5. Detection of the vectors carrying the dimers in tandem:

Nar dimer:

SEQ ID No. 49      primer KS 620: 5' CGC GCG TAA TAC GAC TCA CT 3';

SEQ ID No. 46      primer PCV 5: 5' GTG TGC TCG ACA TTG GTG TG 3';

Kpn dimer:

SEQ ID No. 49      primer KS 620: 5' CGC GCG TAA TAC GAC TCA CT 3';

SEQ ID No. 48 primer PCV 6: 5'CTC GCA GCC ATC TTG GAA TG 3';

6. Differential detection:

The pairs of primers used are those described, for example, in paragraphs 4 and 5 above.

5 The procedures using the pairs or primers described in paragraphs 4 and 5 are of particular interest for differentially detecting the circular monomeric forms of specific replicative forms of the virion or of the DNA in replication and the dimeric forms found in the so-called in-tandem molecular constructs.

10 The in-tandem constructs of the viral genome (dimers) such as the constructs used for the preparation of the pBS KS + tandem PCV Kpn I vector, deposited at the CNCM under the number I-1891, 3 July 1997 (E. coli transformed by said vector) are very interesting for their use in methods of production in sufficient quantity of an inoculum formed of DNA, intended for the virus production, this in the absence of a satisfactory virus production protocol in a cell system. These said  
15 methods of production using these in-tandem constructs of the viral genome will allow the virulence factors to be studied by mutation and by way of consequence will be able to be used for the production of a collection of viruses carrying the mutations indicated in the construction of vectors which will have the appropriate tropism and virulence. These vectors with autoreplicative structure have the sought  
20 gene transfer properties, especially for their applications in gene therapy, and in vaccinology.

Western-blot analysis of recombinant proteins of the PWD circovirus of type A

The results were obtained using a specific antiserum of the PWD circovirus produced during test 1 (cf. Figure 1).

25 Type of products analyzed.

The analyses were carried out on cell extracts of Sf9 cells obtained after infection by the recombinant baculovirus PCV ORF 1.



The culture of Sf9 cells was carried out in a 25 cm<sup>2</sup> Petri dish according to the standard culture methods for these cells. After centrifugation, the cell pellets are taken up with 300 µl of PBS buffer (phosphate saline buffer).

#### Electrophoresis (PAGE-SDS)

5 The electrophoresis is carried out on the cell extracts of Sf9 cells obtained previously on 5 samples (cf. Table 1 below) under the following conditions:

% polyacrylamide gel: 8%; conditions: denaturing

Voltage: 80 V; duration: 135 mn.

10 Table 1: Nature of the samples subjected to electrophoresis

Well No.	1	2	3	4	5
Sample applied	PM Rainbow	Raoul 24 h	Raoul 48 h	Raoul 72 h	Raoul 96 h
µl of sample	10	15	15	15	15
µl of Laemmli 4X	0	5	5	5	5

#### Legends to Table 1:

Laemmli 4X: loading buffer

PM Rainbow: molecular-weight markers (35, 52, 77, 107, 160 and 250 kD)

15 Raoul 24 h, 48 h, 72 h and 96 h: expression products of the ORF1 of the PWD circovirus of type A.

#### Western blot

20 After electrophoresis, the bands obtained in the different wells are transferred to nitrocellulose membrane for 1 h at 100 v in a TGM buffer (tris-glycine-methanol).

The Western blot is carried out under the following conditions:

1) Saturation with a solution containing 5% of skimmed milk; 0.05% of Tween 20 in a TBS 1X buffer (tris buffer saline) for 30 min.

25 2) 1st antibody:

10 ml of PWD anticircovirus antibody of type A are added diluted to 1/100; then the reaction mixture is incubated for one night at 4°C. Three washes of 10 min in TBS 1X are carried out.

3) 2nd antibody:

5 10 ml of pig rabbit P164 antibody anti-immunoglobulins, coupled to peroxidase (Dakopath) are added diluted to 1/100, then the reaction medium is incubated for 3 hours at 37°C. Three washes of 10 min in TBS 1X are carried out.

4) Visualization

10 The substrate 4-chloro-1-naphthol in the presence of oxygenated water is used for visualization.

Results

The results are shown in Figure 7.

15 Kinetics of appearance of antibodies specific for the REP recombinant protein of the PWD circovirus of type A expressed in baculovirus after infection of pigs by the PWD circovirus of type A (test 4, cf. Figure 1)

After infection of the pigs, a sample of serum of each of the infected pigs is taken at different periods expressed in the table by the date of taking (carried out here in the same year) and is then analyzed by Western blot.

20 The visualization of the specific antibodies is carried out in the manner described previously.

The results obtained are shown by Table 2 below.

Table 2: Kinetics of appearance of specific antibodies

Sample	Pigs	10/6	16/06	23/06	01/07	08/07	15/07	21/07
A3	1						Neg.	
Control	2						Neg.	
B2 Infec.	1	Neg.	Neg.	Neg.	+	+	++	+++
RP+	2	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
	3	Neg.	Neg.	Neg.	Neg.	+	+	+
	4	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	++

Legends to Table 2:

- 5 A3 control: uninfected control animals;  
B2 Infec. RP+: animals infected with pig kidney (PK) cells containing the  
circovirus;  
Neg.: negative;  
+, ++, +++: intensity scale of the positive reaction;  
10/06, 16/06, 23/06, 01/07, 08/07, 15/07, 21/07: dates expressed in day/month  
on which the different withdrawals of serum were carried out.

10 EXAMPLE 2: Cloning, sequencing and characterization of the type B PWD  
circovirus (PCVB)

The techniques used for cloning, sequencing and characterization of the type  
B PWD circovirus (PCVB) are those used in Example 1 above for the type A PWD  
circovirus (PCVA).

15 The nucleic sequence of the strand of (+) polarity of the genome of the  
PWD circovirus of type B (or PCVB) is represented by the sequence SEQ ID No.  
15 in the sequence listing, the nucleic sequence of the strand of (-) polarity of the  
genome of the PWD circovirus of type B (or PCVB) being represented by the  
nucleic sequence 3' → 5' of Figure 8 or by the sequence SEQ ID No. 19  
20 (represented according to the orientation 5' → 3') in the sequence listing.

The amino acid sequences SEQ ID No. 24, SEQ ID No. 26 and SEQ ID No.  
28 of the sequence listing respectively represent the sequences of the proteins  
encoded by the nucleic sequences of the 3 open reading frames SEQ ID No. 23  
(ORF'1), corresponding to the REP protein, SEQ ID No. 25 (ORF'2) and SEQ ID  
25 No. 27 (ORF'3), determined from the sequence SEQ ID No. 15 of the strand of (+)  
polarity or from the nucleic sequence SEQ ID No. 19 of the strand of (-) polarity of  
the genome of the PWD circovirus of type B.

30 EXAMPLE 3: Comparative analysis of nucleotide sequences (ORF1, ORF2 and  
genomic) and amino acid sequences encoded by the ORF1 and the ORF2 of the  
PWD circoviruses of type A (PCVA) and of type B (PCVB)

The results expressed in % of homology are shown in Tables 3 and 4 below.

**Table 3: Compared analysis of the amino acid sequences**

% homology	ORF1	ORF2
PCVA/PCVB	80.4	56.2

**Table 4: Compared analysis of the nucleotide sequences**

% homology	Genomic	ORF1	ORF2	The remainder
PCVA/PCVB	70.4	80.4	60.1	66.1

**EXAMPLE 4: Observation of the disease and reproduction of the disease under experimental conditions**

**a) Test No. 1: Observation of the disease**

The objective is to take breeding animals at the start of disease and to place them under experimental conditions to follow the progression of the pathology and describe all the clinical signs thereof. This first test was carried out on 3 breeding pigs aged 10 weeks of which 2 were already ill (suffering from wasting), and on 3 other pigs aged 13 weeks, not having signs of disease. The clinical observation was spread over a period of 37 days. Two pigs of 10 weeks wasted rapidly (pigs 1 and 2, Figure 9) and had to be painlessly killed 5 and 6 days after their arrival. A single pig exhibited hyperthermia over 5 days and diarrhea. Two other pigs exhibited dyspnea and cough, of which one additionally had hyperthermia, greater than 41°C, for the two first days of its stay. Another pig had retarded growth in the second week (pig 6, Figure 9), without any other clinical sign being recorded. On the lesional level, 5 pigs out of 6 exhibited macroscopic lesions of gray pneumonia, the sixth exhibited cicatricial lesions on the lung.

**b) Test No. 2: Reproduction of the disease from inocula prepared in farm pigs.**

The two sick pigs in test 1 served to prepare inocula which were tested in test 2 on specific-pathogen-free (SPF) pigs. The SPF pigs were aged 9 weeks at the time of inoculation. The clinical and lesional results are shown in Table 5.

**Table 5:** Summary of the measurements carried out during experimental reproduction of PWD. (The values of the control animals are reported in brackets, the underlined values indicate a difference between infected animals and control animals)

Measurement	Test	2	3	4	5	6	7
Status of the pigs		SPF	SPF	SPF	SPF	Conventional	Conventional
Age		CNEVA	field	CNEVA	CNEVA	5 weeks	6-7 weeks
Number		9 weeks	6 weeks	5 weeks	5 weeks	8	8
Inoculation route		Intratracheal route	Intratracheal route	Intratracheal + intramuscular route	Intratracheal + intramuscular route	Intratracheal + intramuscular route	Intratracheal + intramuscular route
Inoculum titer per pig		ND*	ND*	10 <sup>4.53</sup> TCID <sub>50</sub> per ml: 1 ml IM + 5 ml IT	10 <sup>4.53</sup> TCID <sub>50</sub> per ml: 1 ml IM + 5 ml IT	10 <sup>4.53</sup> TCID <sub>50</sub> per ml: 1 ml IM + 5 ml IT	10 <sup>4.53</sup> TCID <sub>50</sub> per ml: 1 ml IM + 5 ml IT
Start of hyperthermia		10 days post-infection	9-13 days post-infection	12-13 days post-infection	9-14 days post-infection	8-12 days post-infection	12 days post-infection
% of pigs in hyperthermia**		100%	83%	92%	100%	75%	88%
Number of days of hyperthermia per pig**		7	4.5	3.3	5.8	7.5	11.6

Maximum temperatures	40.4 to 41.7°C	40.6 to 42.3°C	40.2 to 41.6°C	40.3 to 40.8°C	40.6 to 42°C	40.2 to 41.9°C
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Measurement	Test	2	3	4	5	6	7
***							
Hyperthermia****							
% per week							
W1		3.5 (3.5)	17 (36)	7 (5)	37 (17)	16 (17)	20 (28)
W2		42 (3.5)	7 (13)	13 (1)	21 (3)	52 (10)	37 (28)
W3		35 (3.5)	33 (10)	28 (7)	62 (2)	34 (12)	79 (17)
W4		21 (3.5)	28 (7)	5 (0)	6 (3)	25 (22)	55 (3)
DMG:							
W1		928 (1053)	417 (357)	564 (620)	650 (589)	401 (407)	509 (512)
W2		678 (1028)	428 (617)	503 (718)	612 (584)	294 (514)	410 (310)
W3		661 (1000)	771 (642)	381 (657)	520 (851)	375 (586)	435 (440)
W4		786 (1100)	550 (657)	764 (778)	641 (696)	473 (610)	451 (681)
Contact pigs		Yes to 100%	Yes to 75%	Not tested	Not tested	Not tested	Not tested
transmission							
% of pulmonary lesions		25	75	0	25	25	12
% of ganglionic lesions		17	33	67	25	50	12

\* ND: not determined,

\*\* hyperthermia when the temperature is greater than 40°C,

\*\*\* range of maximum temperatures recorded at the individual level,

\*\*\*\* the percentage corresponds to the number of temperature recordings greater than 40°C divided by the total number of temperature recordings in the week on all of the pigs.

In this test, there was no wasting, at the very most a retardation of the growth in the second, third or fourth week after infection. These data illustrate that certain breeding conditions probably favor the expression of the disease.

c) Tests No. 3 to No. 7: Reproduction of the experimental tests

5 The increase in the number of the experimental tests on pigs had the mastering and better characterization of the experimental model as an objective. All of the results are presented in Table 5.

Under the experimental conditions, PWD is thus characterized by a long incubation, of 8 to 14 days, true hyperthermia over 2 to 8 days, a decrease in food  
10 consumption and a retardation of the increase in weight on the second, third or fourth week post-infection. The lesional table associated with this clinical expression includes, in the main, ganglionic hypertrophy and lesions of pneumonia.

Conclusion

The perfection of this experimental model allows the direct etiological role  
15 of the PWD circovirus in the disease to be indisputably demonstrated. In addition, this model is an indispensable tool for the understanding of pathogenic mechanisms and the study of future vaccine candidates.

EXAMPLE 5: Demonstration of the vaccine composition protective efficacy  
20 produced from nucleic fragments of PWD circovirus sequence

1) Animals used for the study

Piglets having the PWD disease, reproduced under experimental conditions described in paragraph c) of Example 4, were used in a protocol for evaluating the vaccine composition efficacy, comprising nucleic fragments of PWD circovirus  
25 sequence.

2) Tested vaccine composition and vaccination protocol

a) Components used for the study

The plasmids were obtained from the pcDNA3 plasmid of INVITROGENE  
- pcDNA3ORF- plasmids



comprising a nucleic acid fragment SEQ ID No. 23 (ORF'1) and an insert comprising the nucleic acid fragment SEQ ID No. 25 (ORF'2).

- Adjuvant

The adjuvant supplied by the Seppic Company, a subsidiary of AIR LIQUIDE, is the adjuvant corresponding to the reference AIF SEPPIC.

b) Vaccination protocol

Weaned piglets aged 3 weeks are divided into four batches A, B, C and D each comprising 8 piglets.

Batches A, B and C, aged 3 weeks, each receive a first injection (injection M1) of 1 ml containing 200 micrograms of plasmids (naked DNA) in PBS, pH: 7.2, by the intramuscular route for each of the plasmids mentioned below for each batch, then, at the age of 5 weeks, a second injection (injection M2) comprising these same plasmids. A third injection is carried out simultaneously on the other side of the neck. This third injection comprises 1 ml of a suspension containing  $5 \cdot 10^6$  cells infected by recombinant baculoviruses and 1 ml of AIF SEPPIC adjuvant.

Batch A (F1) (control batch):

- first injection

pcDNA3ORF1- plasmid, pcDNA3ORF2- plasmid and GMCSF+ plasmid.

- second and third injection (simultaneous)

pcDNA3ORF1- plasmid, pcDNA3ORF2- plasmid and GMCSF+ plasmid;

Cells transformed by baculoviruses not containing any nucleic acid insert coding for a PWD circovirus protein;

AIF SEPPIC adjuvant.

Batch B (F2) (control batch):

- first injection

pcDNA3ORF1- plasmid, pcDNA3ORF2- plasmid and GMCSF+ plasmid;

- second and third injection (simultaneous)

pcDNA3ORF1- plasmid, pcDNA3ORF2- plasmid and GMCSF+ plasmid;

Cells transformed by baculoviruses not containing any nucleic acid insert coding for a PWD circovirus protein;

AIF SEPPIC adjuvant.

Batch C (F3):

-first injection

5 pcDNA3ORF1+ plasmid, pcDNA3ORF2+ plasmid and GMCSF+ plasmid;

- second and third injection (simultaneous)

pcDNA3ORF1+ plasmid, pcDNA3ORF2+ plasmid and GMCSF+ plasmid;

10 Cells transformed by BAC ORF1+ and BAC ORF2+ recombinant baculoviruses capable of respectively expressing the Rep protein of sequence SEQ ID No. 24 and the protein of sequence SEQ ID No. 26 of the PWD circovirus of TYPE B.

Batch D (F4) (control batch): no injection

15 The batches of piglets B, C and D are infected (tested) at the age of 6 weeks although batch A is not subjected to the test.

3) Observation of the batches

- 20
- counting of coughing/sneezing: 15 minutes/batch/day;
  - consistency of fecal matter: every day;
  - regular recordings: weekly taking of blood, weighing;
  - weighing of food refuse: 3 times per week;
  - calculation of the daily mean gain in weight (dmg);

25 The daily mean gains were calculated for each of the batches over a period of 28 days following testing (cf. Figure 10), an intermediate calculation of the dmg was likewise carried out for each of the batches over the first and second periods of 14 days. The results obtained are reported below in Table 6.

These plasmids are plasmids which do not carry a PWD circovirus nucleic acid insert and are used as a negative control plasmid.

- pcDNA3ORF1+ plasmid and pcDNA3ORF2+ plasmid

5 The pcDNA3ORF1+ and pcDNA3ORF2+ plasmids are plasmids which carry a nucleic acid insert of the sequence of the PWD circovirus of TYPE B, respectively an insert comprising the nucleic acid fragment SEQ ID No. 23 (ORF'1) coding for the Rep protein of sequence SEQ ID No. 24 and an insert comprising the nucleic acid fragment SEQ ID No. 25 (ORF'2) coding for the protein of sequence SEQ ID No. 26, probably corresponding to the capsid protein, these nucleic  
10 constructs comprising the ATG initiation codon of the coding sequence of the corresponding protein.

- GMCSF+ plasmid

GM-CSF (granulocyte/macrophage colony stimulating factor) is a cytokine which occurs in the development, the maturation and the activation of macrophages,  
15 granulocytes and dendritic cells which present an antigen. The beneficial contribution of the GM-CSF in vaccination is considered to be a cellular activation with, especially, the recruitment and the differentiation of cells which present an antigen.

This pcDNA3-GMCSF+ plasmid carries a nucleic acid insert coding for the granulocyte/macrophage colony stimulation factor, the GM-CSF protein.  
20

The gene coding for this GM-CSF protein was cloned and sequenced by Inumaru et al. (Immunol. Cell Biol., 1995, 73 (5), 474-476). The pcDNA3-GMCSF+ plasmid was obtained by Dr. B. Charley of INRA of Jouy-en-Josas (78, France).

25 - Recombinant baculoviruses

The so-called ORF- baculoviruses are viruses not carrying any insert comprising a nucleic acid fragment capable of expressing a PWD circovirus protein.

The so-called ORF1+ (BAC ORF1+) or ORF2+ (BAC ORF2+) baculoviruses are recombinant baculoviruses respectively carrying an insert

Table 6: Daily mean gains

	F1	F2	F3	F4
d0-d14	411 g	450 g	511 g	461 g
d14-d28	623 g	362 g	601 g	443 g
d0-d28	554 g	406 g	556 g	452 g

- Measurement of hyperthermia

The measurement of hyperthermia, of greater than 41°C (cf. Figure 11) and greater than 40.2°C, was carried out for each of the batches over a total period of 28 days following testing. The results obtained, corresponding to the ratio expressed as a percentage between the number of recordings of heat of greater than 41°C (or greater than 40.2°C) and the total number of recordings of heat carried out on all of the pigs per one-week period are reported below in Tables 7 and 8, respectively for the hyperthermia measurements of greater than 41°C and greater than 40.2°C.

Table 7: Hyperthermia > 41°C

	F1	F2	F3	F4
W1	4.1	0.	0.	0.
W2	10.7	16.	0.	8.9
W3	4.7	27.	0.	45.
W4	0.	0.	0.	7.5

Table 8: Hyperthermia > 40.2

	F1	F2	F3	F4
W1	29.1	10.41	29.1	20.8
W2	28.5	39.2	10.7	37.5
W3	14.3	68.7	25.0	81.2
W4	3.3	17.5	20.0	55

#### 4) Conclusion

The recordings carried out clearly show that the animals which received the three injections of a vaccine composition comprising nucleic acid fragments of PWD circovirus according to the invention and/or capable of expressing recombinant proteins of PWD circovirus, in particular of type B, did not exhibit hyperthermia (cf. Figure 10). These animals additionally did not experience a decline in their growth, the dmgs being comparable to those of uninfected control animals (cf. Figure 9). They did not exhibit any particular clinical sign.

These results demonstrate the efficacious protection of the piglets against infection with a PWD circovirus of the invention, the primary agent responsible for PWD or FPW, provided by a vaccine composition prepared from a nucleic acid fragment of the nucleic sequence of PWD circovirus according to the invention, in particular of type B, and/or from recombinant proteins encoded by these nucleic acid fragments.

These results in particular show that the proteins encoded by the ORF1 and ORF2 of PWD circovirus according to the invention are immunogenic proteins inducing an efficacious protective response for the prevention of infection by a PWD circovirus.

EXAMPLE 6: Serological diagnosis of PWD circovirus by immunodetermination using recombinant proteins or synthetic peptides of PWD circovirus

#### A - Serological diagnosis with recombinant proteins

The identification and the sequencing of porcine PWD circovirus allow recombinant proteins of PWD circovirus to be produced by the techniques of genetic recombination well known to the person skilled in the art.

By these techniques, recombinant proteins encoded, in particular, by the ORF'2 of the PWD circovirus, type B, were expressed by transformed Sf9 insect cells and then isolated.

These recombinant proteins encoded by the ORF'2 are extracted, after culture of the transformed Sf9 cells, by thermal cell lysis by means of 3 cycles of

freezing/thawing to  $-70^{\circ}\text{C}/+37^{\circ}\text{C}$ . Healthy Sf9 cells or nontransformed control Sf9 cells are also lyzed.

These two antigenic fractions originating from nontransformed-control Sf9 cells and Sf9 cells expressing the ORF'2 are precipitated at  $4^{\circ}\text{C}$  by a 60% plus or minus 5% saturated ammonium sulfate solution. Determination of total proteins is carried out with the aid of the Biorad kit. 500 ng of control Sf9 proteins and of semipurified Sf9 proteins expressing the ORF'2, in solution in 0.05 M bicarbonate buffer pH 9.6, are passively adsorbed at the bottom of 3 different cupules of a Nunc Maxisorp microplate by incubation for one night at  $+4^{\circ}\text{C}$ .

The reactivity of pig sera with respect to each of these antigenic fractions is evaluated by an indirect ELISA reaction of which the experimental protocol is detailed below:

- Saturation step: 200  $\mu\text{l}$ /cupule of PBS1X/3% semi-skimmed milk, 1 h 30 incubation at  $37^{\circ}\text{C}$ .

- Washing: 200  $\mu\text{l}$ /cupule of PBS1X/Tween 20: 0.05%, 3 rapid washes.

- Serum incubation step: 100  $\mu\text{l}$ /cupule of serum diluted to 1/100 in PBS1X/semi-skimmed milk, 1%/Tween 20: 0.05%, 1 h incubation at  $37^{\circ}\text{C}$ .

- Washing: 200  $\mu\text{l}$ /cupule of PBS1X/Tween 20: 0.05%, 2 rapid washes followed by 2 washes of 5 min.

- Conjugate incubation step: 50  $\mu\text{l}$ /cupule of rabbit anti-pig conjugate diluted to 1/1000 in PBS1X/semi-skimmed milk, 1%/Tween 20: 0.05%, 1 h incubation at  $37^{\circ}\text{C}$ .

- Washing: 200  $\mu\text{l}$ /cupule of PBS1X/Tween 20: 0.05%, 2 rapid washes followed by 2 washes of 5 min.

- Visualization step: 100  $\mu\text{l}$ /cupule of OPD substrate/citrate buffer/ $\text{H}_2\text{O}_2$ , 15 min incubation at  $37^{\circ}\text{C}$ .

- Stopping of reaction: 50  $\mu\text{l}$ /cupule of 1 N  $\text{H}_2\text{SO}_4$ .

- Reading in a spectrophotometer at 490 nm.

### Results

The results obtained are shown below in Table 9.

Table 9

Antigens	Reactivity of Pig Serum not inoculated with Circovirus	Reactivity of Pig Serum inoculated with Circovirus
Purified Sf9 control	0.076	0.088
Sf9 expressing purified ORF'2	0.071	1.035

The results are expressed in optical density measured in a spectrophotometer at 490 nm during analysis by ELISA of the reactivity of pig sera which are or are not inoculated with the type B PWD circovirus according to the protocol indicated above.

#### B - Serological Diagnosis by Synthetic Peptide

The epitopic mapping of the proteins encoded, for example, by the nucleic sequences ORF1 and ORF2 of the two types of PWD circovirus (types A and B) additionally allowed immunogenic circoviral epitopes to be identified on the proteins encoded by the nucleic sequences ORF'1 and ORF'2 as well as the specific epitopes of the protein encoded by the nucleic sequence ORF'2 of the type B PWD circovirus. Four specific epitopes of the type B PWD circovirus and one epitope common to the two types of PWD circovirus situated on the protein encoded by the nucleic sequence ORF'2 were synthesized in peptide form. The equivalent peptides in the circovirus of type A were likewise synthesized. All these peptides were evaluated as diagnostic antigens within the context of carrying out a serological test.

#### Results

The results obtained are shown in Table 10 below.

Table 10: Results of the evaluation as a diagnostic antigen of synthetic peptides encoded by the nucleic sequences ORF2 and ORF'2 of PWD circovirus of type A and B.

Infected pig serum reactivity									
Circovirus B									
Peptide	Type	Position	AA sequence	SPF D0/D54	Conventional 1 D0/D42	Conventional 2 D0/D42	Epitopic specificity		
SEQ ID NO: 29	B	71-85	VDMMRFNINDELPPG	+/-, +++	+/-, +++	-, +++	Circovirus B		
SEQ ID NO: 55	B	70-84	NVNELRFNIGQLPP	+/-, +	+/-, +/-	+/-, -	"		
SEQ ID NO: 30	B	115-129	QGDRGVGSSAVILDD	+/-, +/-	++ , ++	+/-, +	Circovirus B		
SEQ ID NO: 56	A	114-127	TSNQRGVGSTVVIL	+/-, -	-, +/-	+/-, +/-	"		
SEQ ID NO: 31	B	119-134	GVGSSAVILDDNVFTK	-, ++	++ , +++	+/-, ++	"		
SEQ ID NO: 57	A	118-132	RGVGSVVILDANFV	+/-, -	-, +/-	+/-, +/-	"		
SEQ ID NO: 58	B	171-185	FTIDYFQPNKRNQL	-, +/-	-, ++	-, ++	Circovirus A&B		
SEQ ID NO: 59	A	170-184	DQTIDWFQPNKRNQ	+++ ,	+/-, ++	+, ++	"		
SEQ ID NO: 32	B	195-209	VDHVGLGTAFENSIY	-, ++	+++ , +++	+/-, +	Circovirus B		
SEQ ID NO: 60	A	194-208	NVEHTGLGYALQNAT	-, -	-, -	-, -	"		

+/-, +, +, +, +, +. Increasing intensities of the reactivities observed in Spot peptides on a nitrocellulose membrane. The porcine sera tested are from animals experimentally infected with the circovirus of type B within the animal houses of the CNEVA. Samples are taken from the animals before inoculation on d0 and 42 days or 54 days after inoculation, on d42, d54.



**EXAMPLE 7:** Characterization of the specific epitopes of the PWD circovirus of type B

The proteins encoded by the ORF2 of the porcine circoviruses of type A and B were chosen for this study. For each of the ORF2s (types A and B), 56 peptides of 15 amino acids which overlap every 4 amino acids were synthesized, thus covering the whole of the protein (cf. Table 11 below).

**Table 11:** Sequence of amino acids of the 56 peptides of 15 amino acids synthesized from the nucleic sequence ORF'2 (type B) and ORF2 (type A) of PWD circovirus with their corresponding spot number (cf. Figure 12)

Type B ORF'2			Type A ORF2		
	Spot No.	Sequence		Spot No.	Sequence
SEQ ID NO:61	107	HRPRSHLGQILRRRP	SEQ ID NO:84	163	TRPRSHLGNILRRRP
SEQ ID NO:62	108	SHLGQILRRRPWL VH	SEQ ID NO:85	164	SHLGNILRRRPYL VH
SEQ ID NO:63	109	QILRRRPWL VHPRHR	SEQ ID NO:86	165	NILRRRPYL VHPAFR
SEQ ID NO:64	110	RRPWL VHPRHRYRWR	SEQ ID NO:87	166	RRPYL VHPAFRNRYR
SEQ ID NO:65	111	LVHPRHRYRWRKNG	SEQ ID NO:88	167	LVHPAFRNRYRWRRK
SEQ ID NO:66	112	RHRYRWRKNGIFNT	SEQ ID NO:89	168	AFRNRYRWRKGTGIF
SEQ ID NO:67	113	RWRRKNGIFNTRL SR	SEQ ID NO:90	169	RYRWRKGTGIFNSRL
SEQ ID NO:68	114	KNGIFNTRLSRTFGY	SEQ ID NO:91	170	RRKTGIFNSRLSREF
SEQ ID NO:69	115	FNTRLSRTFGYTVKR	SEQ ID NO:92	171	GIFNSRLSREFVLT I
SEQ ID NO:70	116	LSRTFGYTVKR TTVR	SEQ ID NO:93	172	SRLSREFVLTIRGGH
SEQ ID NO:71	117	FGYTVKR TTVRTPSW	SEQ ID NO:94	173	REFVLTIRGGHSQPS
SEQ ID NO:72	118	VKR TTVRTPSWAVDM	SEQ ID NO:95	174	LTIRGGHSOPSWNVN
SEQ ID NO:73	119	TVRTPSWAVDMMRFN	SEQ ID NO:96	175	GGHSQPSWNVNELRF
SEQ ID NO:74	120	PSWAVDMMRFNINDF	SEQ ID NO:97	176	QPSWNVNELRFNIGO
SEQ ID NO:29	121	VDMMRFNINDFLPPG	SEQ ID NO:98	177	NVNELRFNIGQFLPP
SEQ ID NO:75	122	RFNINDFLPPGGGSN	SEQ ID NO:99	178	LRFNIGQFLPPSGGT
SEQ ID NO:76	123	NDFLPPGGGSNPRSV	SEQ ID NO:100	179	IGQFLPPSGGTNPLP
SEQ ID NO:77	124	PPGGGSNPRSVPF EY	SEQ ID NO:101	180	LPPSGGTNPLPLPFQ
SEQ ID NO:78	125	GSNPRSVPF EYYRIR	SEQ ID NO:102	181	GGTNPLPLPFQYYRI
SEQ ID NO:79	126	RSVPF EYYRIRKVKV	SEQ ID NO:103	182	PLPLPFQYYRIRKAK
SEQ ID NO:80	127	FEYYRIRKVKVEFWP	SEQ ID NO:104	183	PFQYYRIRKAKYEFY
SEQ ID NO:81	128	RIRKVKVEFWPCSP I	SEQ ID NO:105	184	YRIRKAKYEFYPRDP
SEQ ID NO:82	129	VKVEFWPCSPITQGD	SEQ ID NO:106	185	KAKYEFYPRDPITSN
SEQ ID NO:83	130	FWPCSPITQGDRGVG	SEQ ID NO:107	186	EFYPRDPITSNQRGV
SEQ ID NO:30	131	SPITQGDRGVGSSAV	SEQ ID NO:108	187	RDPITSNQRGVGSTV
SEQ ID NO:31	132	QGDRGVGSSAVILDD	SEQ ID NO:109	188	TSNQRGVGSTVVILD
SEQ ID NO:110	133	GVGSSAVILDDNFVT	SEQ ID NO:136	189	RGVGSTVVILDANFV
SEQ ID NO:111	134	SAVILDDNFVTKATA	SEQ ID NO:137	190	STVVILDANFVTPST
SEQ ID NO:112	135	LDDNFVTKATALTYD	SEQ ID NO:138	191	ILDANFVTPSTNLAY
SEQ ID NO:113	136	FVTKATALTYDPYVN	SEQ ID NO:139	192	NFVTPSTNLAYDPYI
SEQ ID NO:114	137	ATALTYDPYVNYSSR	SEQ ID NO:140	193	PSTNLAYDPYINYSS
SEQ ID NO:115	138	TYDPYVNYSSRITIT	SEQ ID NO:141	194	LAYDPYINYSSRHTI
SEQ ID NO:116	139	YVNYSSRHTITQPFS	SEQ ID NO:142	195	PYINYSSRHTIRQPF

Type B ORF'2			Type A ORF2		
Spot No.		Sequence	Spot No.		Sequence
SEQ ID NO:117	140	SSRHTITQPFSYHSR	SEQ ID NO:143	196	YSSRIITIRQPFTYHS
SEQ ID NO:118	141	TITQPFSYHSRYFTP	SEQ ID NO:144	197	HTIRQPFTYHSRYFT
SEQ ID NO:119	142	PFSYHSRYFTP KPVL	SEQ ID NO:145	198	QPFTYHSRYFTP KPPE
SEQ ID NO:120	143	HSRYFTP KPVL DFTI	SEQ ID NO:146	199	YHSRYFTP KPPELDQT
SEQ ID NO:121	144	FTP KPVL DFTIDYYFQ	SEQ ID NO:147	200	YFTP KPPELDQTIDWF
SEQ ID NO:122	145	PVL DFTIDYFQPNNK	SEQ ID NO:148	201	KPELDQTIDWFQPNN
SEQ ID NO:123	146	FTIDYFQPNNKRNQL	SEQ ID NO:149	202	DQTIDWFQPNNKRNQ
SEQ ID NO:124	147	YFQPNNKRNQLWLRL	SEQ ID NO:150	203	DWFQPNNKRNQLWLH
SEQ ID NO:125	148	NNKRNQLWLRLQTAG	SEQ ID NO:151	204	PNNKRNQLWLHLNTH
SEQ ID NO:126	149	NQLWLRLQTAGNVDH	SEQ ID NO:152	205	RNQLWLHLNTHTNVE
SEQ ID NO:127	150	LRLQTAGNVDHVGLG	SEQ ID NO:153	206	WLHLNTHTNVEHTGL
SEQ ID NO:128	151	TAGNVDHVGLGTAFE	SEQ ID NO:154	207	NHTNVEHTGLGYAL
SEQ ID NO:32	152	VDHVGLGTAFENSIY	SEQ ID NO:155	208	NVEHTGLGYALQNAT
SEQ ID NO:129	153	GLGTAFENSIYDQEY	SEQ ID NO:156	209	TGLGYALQNATTAQN
SEQ ID NO:130	154	AFENSIYDQEYNIRV	SEQ ID NO:157	210	YALQNATTAQNYVVR
SEQ ID NO:131	155	SIYDQEYNIRVTMYV	SEQ ID NO:158	211	NATTAQNYVVRILTII
SEQ ID NO:132	156	QEYNIRVTMYVQFRE	SEQ ID NO:159	212	AQNYVVRILTIIYVQFR
SEQ ID NO:133	157	IRVTMYVQFRENFNK	SEQ ID NO:160	213	VVRLTIYVQFREIFIL
SEQ ID NO:134	158	MYVQFRENFNKDPPL	SEQ ID NO:161	214	TIYVQFREIFILKDPL
SEQ ID NO:135	159	VQFRENFNKDPPLNP	SEQ ID NO:162	215	YVQFREIFILKDPLNE

These peptides were synthesized according to the "spot" method which consists in simultaneous synthesis of a large number of peptides on a cellulose solid support, each site of synthesis of a peptide constituting a spot (Synt:em, NIMES).

5 This method involves orientation of the peptides on the plate, these being fixed covalently by the carboxy-terminal end. A spot represents approximately 50 nmol of peptide.

The reference of the spots and corresponding peptide sequences is given in Table 11.

10 These membranes were used for immunoreactivity tests with respect to serum of SPF pigs which were or were not infected experimentally with the type B PWD circoviral strain as well as with respect to sera of infected pigs from conventional farms (conventional farms 1 or 2). This study allowed specific immunoreactive peptides of the circovirus of type B corresponding to the spots No.

15 121, No. 132, No. 133 and No. 152 (respectively of amino acid sequences SEQ ID No. 29, SEQ ID No. 30, SEQ ID No. 31 and SEQ ID No. 32) to be demonstrated. An illustration is shown in Figure 12 where the membranes are visualized with an

infected pig serum coming from a conventional farm. Nonspecific immunoreactive peptides of type [lacuna] were likewise demonstrated, among which we shall keep the peptide No. 146 SEQ ID No. 123 which is strongly immunogenic.

A comparison between the peptide sequences of circoviruses of type A and B (Figure 13) indicates a divergence ranging from 20 to 60% for the specific immunoreactive peptides of the type B, and a weaker divergence (13%) between the nonspecific peptides.

EXAMPLE 8: Protection of Swine From Post-Weaning Multisystemic Wasting Syndrome (PMWS) Conferred by Procine Circovirus TypeB (PCV-B) ORF'2 Protein

The ORF'1-encoded protein (REP) and ORF'2-encoded putative capsid protein of PCV-B were expressed, either in insect cells by recombinant baculovirus vectors, or in mammalian cell lines by transfection with plasmidic expression vectors. These two circovirus-derived proteins were detectable in both expression system. As evaluated by weight gains, hyperthermia and absence of lesions following challenge, the pigs were protected against a virulent circovirus challenge after one first DNA immunization with plasmids directing ORF'2 protein and GM-CSF expression and a second injection, 15 days later, with the same plasmid preparation plus the ORF'2 recombinant protein. A lower level of protection was observed when the pigs were vaccinated with ORF'1 protein, as opposed to pigs vaccinated with ORF'2 protein.

A. Development of an experimental model of PMWS in swine:

Eight 3 week-old SPF pigs were inoculated intratracheally (5 ml) and intramuscularly (1 ml).

B. Production and control of PCV-B plasmids:

PCV-B ORF'1 and ORF'2 genes , isolated from PCV-B challenge strain, have been cloned into vector plasmid pcDNA3.1.

All constructs have been validated through a partial sequencing of the PCV-B genes in the final plasmids and expression control by immunoperoxidase on PK15 cells respectively transfected with each plasmid, using swine polyclonal antibodies.

Plasmid encoding GM-CSF has been co-administered.

5 C. Construction of recombinant baculoviruses:

ORF'1 and ORF'2 proteins were expressed under polyhedrin promoter control. Recombinant proteins were detected by western-blot using swine polyclonal antibodies.

D. Vaccination and challenge:

10 Four groups of 7 pigs were vaccinated intramuscularly at day 0 (Do), two weeks later, they received the same plasmid preparation plus the recombinant baculovirus.

E. Monitoring:

15 All groups of pigs were housed in isolated experimental units with air filtration and low air pressure. Clinical observations and rectal temperatures were recorded every day. The pigs were weighed weekly.

F. Conclusions

20 Expression of PCV-B ORF'2 or PCV-B ORF'1 in swine resulted in a significantly enhanced level of protection as evaluated by weight evolution and body temperature evolution following challenge with PCV-B circovirus. These results are summarized in Figures 14 and 15.

25 The invention described herein may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The specific embodiments previously described are therefore to be considered as illustrative of, and not limiting, the scope of the invention. Additionally, the disclosure of all publications and patent applications cited above and below, including International Patent Application No. PCT/FR98/02634, filed December 4, 1998, and published as

International Publication No. WO 99/29871 on June 17, 1999, are expressly incorporated herein by reference in their entireties to the same extent as if each were incorporated by reference individually.

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**We Claim:**

1. A vaccine comprising a nucleotide sequence of the genome of Porcine circovirus type B, or a homologue or fragment thereof, and an acceptable pharmaceutical or veterinary vehicle.

2. A vaccine according to claim 1, wherein the nucleotide sequence is selected from SEQ ID No. 15 or SEQ ID No. 19.

3. A vaccine according to claim 1, wherein the homologue has at least 80% sequence identity to SEQ ID No. 15 or SEQ ID No. 19.

4. A vaccine according to claim 1, wherein the nucleotide sequence is selected from SEQ ID No. 23 or SEQ ID No. 25, or a homologue or fragment thereof.

5. A vaccine according to claim 4, wherein the homologue has at least 80% sequence identity to SEQ ID No. 23 or SEQ ID No. 25.

6. A vaccine according to claim 4, wherein the nucleotide sequence is SEQ ID No. 25.

7. A vaccine comprising a polypeptide encoded by a nucleotide sequence of the genome of PCVB, or a homologue or fragment thereof, and an acceptable pharmaceutical or veterinary vehicle.

8. A vaccine according to claim 7, wherein the homologue has at least 80% sequence identity to SEQ ID No. 15 or SEQ ID No. 19.

9. A vaccine according to claim 7, wherein the nucleotide sequence is selected from SEQ ID No. 23 or SEQ ID No. 25, or a homologue or fragment thereof.

10. A vaccine according to claim 9, wherein the homologue has at least 80% sequence identity to SEQ ID No. 23 or SEQ ID No. 25.

11. A vaccine according to claim 9, wherein the nucleotide sequence is SEQ ID No. 25.

12. A vaccine according to claim 7, wherein the polypeptide has the amino acid sequence of SEQ ID No. 24 or SEQ ID No. 26.

13. A vaccine according to claim 12, wherein the polypeptide has the amino acid sequence of SEQ ID No. 26.

14. A vaccine according to claim 7, wherein the homologue has at least 80% sequence identity to SEQ ID No. 24 or SEQ ID No. 26.

15. A vaccine according to claim 14, wherein the homologue has at least 80% sequence identity to SEQ ID No. 26.

16. A vaccine according to claim 7, wherein the polypeptide has the amino acid sequence of SEQ ID No. 29, SEQ ID No. 30, SEQ ID No. 31, or SEQ ID No. 32.

17. A vaccine comprising a vector and an acceptable pharmaceutical or veterinary vehicle, the vector comprising a nucleotide sequence of the genome of Porcine circovirus type B, or a homologue or fragment thereof.

18. A vaccine according to claim 17, further comprising a gene coding for an expression product capable of inhibiting or retarding the establishment or development of a genetic or acquired disease.

19. A vaccine comprising a cell and an acceptable pharmaceutical or veterinary vehicle, wherein the cell is transformed with a nucleotide sequence of the genome of Porcine circovirus type B, or a homologue or fragment thereof.

20. A vaccine according to claim 1, further comprising an adjuvant.

21. A vaccine comprising a pharmaceutically acceptable vehicle and a single polypeptide, wherein the single polypeptide consists of SEQ ID No. 26.

22. A method of immunizing a mammal against piglet weight loss disease comprising administering to a mammal an effective amount of the vaccine of any one of claims 1-21.

**Abstract of the Invention**

The genome sequences and the nucleotide sequences coding for the PWD circovirus polypeptides, such as the circovirus structural and non-structural polypeptides, vectors including the sequences, and cells and animals transformed by the vectors are provided. Methods for detecting the nucleic acids or polypeptides, and kits for diagnosing infection by a PWD circovirus, also are provided. Method for selecting compounds capable of modulating the viral infection are further provided. Pharmaceutical, including vaccines, compositions for preventing and/or treating viral infections caused by PWD circovirus and the use of vectors for preventing and/or treating diseases also are provided.

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Leu Ser Leu Phe Cys Tyr His Ile Val Met Val Phe Ile Phe Ile His  
 305 310 315 320

Leu Glu Gly Leu Ser Gly Ile Leu Ile Val His Lys Ser Thr Leu Pro  
 325 330 335

His Asn Phe Gly Leu Trp Leu His Phe Gly Ala His Ser Pro Gly Leu  
 340 345 350

Cys Ala Arg His Trp Cys Gly Tyr Leu Asn Gly Ala Thr Ala Gly Phe  
 355 360 365

Phe Tyr Tyr Leu Ala Gly Thr Asn Gln Leu Phe Gly Leu Ala Leu Val  
 370 375 380

Trp Gly Ser Thr Trp Ser Gly Arg Arg Ala Ala Leu Trp Cys Gly Gly  
 385 390 395 400

Arg Ser Ser Tyr Arg Gly His Arg Pro Ser Trp Trp Arg Gly Leu Gln  
 405 410 415

Ser Trp His Pro Arg Gln Gln Trp Thr Gln His Leu Phe Asp Arg Trp  
 420 425 430

a3



Gly Leu Trp Gly Lys Ile His Ile Pro Phe Tyr Gly Ser Ile Gly Lys  
435 440 445

Val Gly Val Gly Gly Trp Cys Arg Leu Arg Gly Gly Gly Thr Gly Arg  
450 455 460

Cys Ile Ser Ala Arg His Ser Lys Met Ala Ala Ser Val Leu Leu Leu  
465 470 475 480

Trp Val Gln Ile Leu Lys Gly Gly Asn Arg Tyr Pro Ser Phe Gly Ala  
485 490 495

Ile Cys Asn Gly Phe Arg Arg Gly Val Pro Asn Met Val Phe Ser Gly  
500 505 510

Gly Cys Phe Gln Asp Gly Cys Gly Gly Gly Ser Val Phe Cys Gly Asn  
515 520 525

Ala Ser Leu Ala Thr Ser Ser Tyr Lys Ser Glu Arg Ser Ala Leu Leu  
530 535 540

Tyr  
545

<210> 3

<211> 577

<212> PRT

<213> Type A PWD circovirus

<400> 3

Pro Ala His Phe Gly Ser Gly Ser Thr Ser Ala Ala Ser Val Lys Met  
1 5 10 15

Pro Ser Lys Lys Ser Gly Pro Gln Pro His Lys Arg Trp Val Phe Thr  
20 25 30

Leu Asn Asn Pro Ser Glu Glu Glu Lys Asn Lys Ile Arg Glu Leu Pro  
35 40 45

Ile	Ser	Leu	Phe	Asp	Tyr	Phe	Val	Cys	Gly	Glu	Glu	Gly	Leu	Glu	Glu		
50						55					60						
Gly	Arg	Thr	Pro	His	Leu	Gln	Gly	Phe	Ala	Asn	Phe	Ala	Lys	Lys	Gln		
65					70					75					80		
Thr	Phe	Asn	Lys	Val	Lys	Trp	Tyr	Phe	Gly	Ala	Arg	Cys	His	Ile	Glu		
				85					90					95			
Lys	Ala	Lys	Gly	Thr	Asp	Gln	Gln	Asn	Lys	Glu	Tyr	Cys	Ser	Lys	Glu		
			100					105					110				
Gly	His	Ile	Leu	Ile	Glu	Cys	Gly	Ala	Pro	Arg	Asn	Gln	Gly	Lys	Arg		
	115						120					125					
Ser	Asp	Leu	Ser	Thr	Ala	Val	Ser	Thr	Leu	Leu	Glu	Thr	Gly	Ser	Leu		
	130					135					140						
Val	Thr	Val	Ala	Glu	Gln	Phe	Pro	Val	Thr	Tyr	Val	Arg	Asn	Phe	Arg		
145					150					155					160		
Gly	Leu	Ala	Glu	Leu	Leu	Lys	Val	Ser	Gly	Lys	Met	Gln	Lys	Arg	Asp		
			165						170					175			
Trp	Lys	Thr	Ala	Val	His	Val	Ile	Val	Gly	Pro	Pro	Gly	Cys	Gly	Lys		
			180					185					190				
Ser	Gln	Trp	Ala	Arg	Asn	Phe	Ala	Glu	Pro	Arg	Asp	Thr	Tyr	Trp	Lys		
	195					200						205					
Pro	Ser	Arg	Asn	Lys	Trp	Trp	Asp	Gly	Tyr	His	Gly	Glu	Glu	Val	Val		
	210					215					220						
Val	Leu	Asp	Asp	Phe	Tyr	Gly	Trp	Leu	Pro	Trp	Asp	Asp	Leu	Leu	Arg		
225					230					235					240		
Leu	Cys	Asp	Arg	Tyr	Pro	Leu	Thr	Val	Glu	Thr	Lys	Gly	Gly	Thr	Val		
			245						250					255			
Pro	Phe	Leu	Ala	Arg	Ser	Ile	Leu	Ile	Thr	Ser	Asn	Gln	Ala	Pro	Gln		
			260					265					270				
Glu	Trp	Tyr	Ser	Ser	Thr	Ala	Val	Pro	Ala	Val	Glu	Ala	Leu	Tyr	Arg		
		275					280					285					
Arg	Ile	Thr	Thr	Leu	Gln	Phe	Trp	Lys	Thr	Ala	Gly	Glu	Gln	Ser	Thr		
	290					295					300						
Glu	Val	Pro	Glu	Gly	Arg	Phe	Glu	Ala	Val	Asp	Pro	Pro	Cys	Ala	Leu		
305					310					315					320		
Phe	Pro	Tyr	Lys	Ile	Asn	Tyr	Val	Phe	Phe	Val	Ile	Thr	Ser	Trp	Phe		
				325					330					335			

Leu Phe Leu Phe Ile Arg Val Phe Gln Asp Lys Phe Ser Glu Leu Tyr  
 340 345 350  
 Ile Asn Ser Gln Pro Tyr His Ile Ile Leu Gly Cys Gly Cys Ile Leu  
 355 360 365  
 Glu Arg Ile Ala Gln Ala Cys Val Leu Asp Ile Gly Val Gly Ile Met  
 370 375 380  
 Glu Pro Gln Leu Val Ser Phe Ile Ile Trp Leu Glu Pro Ile Asn Cys  
 385 390 395 400  
 Leu Val Leu Trp Phe Gly Gly Glu Val Pro Gly Val Val Gly Lys Gly  
 405 410 415  
 Leu Pro Tyr Gly Val Ala Gly Gly Val Val Asn Ile Gly Val Ile Gly  
 420 425 430  
 Gln Val Gly Gly Gly Gly Tyr Lys Val Gly Ile Gln Asp Asn Asn Ser  
 435 440 445  
 Gly Pro Asn Thr Ser Leu Ile Arg Gly Asp Gly Val Ser Gly Val Lys  
 450 455 460  
 Phe Ile Phe Ser Leu Ser Asn Thr Val Val Leu Glu Arg Gly Val Gly  
 465 470 475 480  
 Ala Ala Gly Gly Glu Glu Leu Ala Asp Val Glu Ser Gln Leu Val Asn  
 485 490 495  
 Ile Pro Arg Trp Leu Arg Val Ser Ser Ser Tyr Gly Glu Tyr Lys Phe  
 500 505 510  
 Ser Arg Lys Ala Gly Ile Glu Asp Thr Arg Leu Ser Ala Pro Ser Val  
 515 520 525  
 Thr Val Ser Glu Gly Gly Val Tyr Gln Ile Trp Ser Ser Pro Glu Asp  
 530 535 540  
 Val Ser Lys Met Ala Ala Gly Ala Gly Pro Ser Ser Ala Val Thr Pro  
 545 550 555 560  
 Pro Trp Pro Arg His Pro Ile Lys Val Lys Glu Val Arg Cys Cys Ser  
 565 570 575

Ile

<210> 4

<211> 553

<212> PRT

<213> Type A PWD circovirus

96

<400> 4

Gln	Arg	Thr	Ser	Ala	Ala	Ala	Ala	Pro	Arg	Gln	Arg	Gln	Lys	Cys	Gln	
1				5					10					15		
Ala	Arg	Lys	Ala	Ala	Arg	Asn	Pro	Ile	Arg	Gly	Gly	Cys	Ser	Pro	Leu	
		20					25						30			
Leu	Pro	Arg	Arg	Arg	Lys	Thr	Lys	Tyr	Gly	Ser	Phe	Gln	Ser	Pro	Phe	
	35					40						45				
Leu	Ile	Ile	Leu	Phe	Val	Ala	Arg	Lys	Val	Trp	Lys	Arg	Val	Glu	Leu	
	50					55					60					
Leu	Thr	Ser	Arg	Gly	Leu	Arg	Ile	Leu	Leu	Arg	Ser	Arg	Leu	Leu	Thr	
65					70					75					80	
Arg	Ser	Gly	Ile	Leu	Val	Pro	Ala	Ala	Thr	Ser	Arg	Lys	Arg	Lys	Glu	
				85					90						95	
Pro	Thr	Ser	Arg	Ile	Lys	Asn	Thr	Ala	Val	Lys	Lys	Ala	Thr	Tyr	Leu	
			100					105						110		
Ser	Ser	Val	Glu	Leu	Arg	Gly	Thr	Arg	Gly	Ser	Ala	Ala	Thr	Cys	Leu	
		115					120					125				
Leu	Leu	Val	Pro	Phe	Trp	Arg	Arg	Gly	Leu	Trp	Leu	Pro	Ser	Ser	Phe	
	130					135					140					
Leu	Arg	Met	Glu	Ile	Ser	Ala	Gly	Trp	Leu	Asn	Phe	Lys	Ala	Gly	Arg	
145					150					155					160	
Cys	Arg	Ser	Val	Ile	Gly	Arg	Gln	Leu	Tyr	Thr	Ser	Trp	Ala	Arg	Pro	
				165					170						175	
Val	Val	Gly	Arg	Ala	Ser	Gly	Pro	Val	Ile	Leu	Leu	Ser	Leu	Gly	Thr	
			180					185						190		
Pro	Thr	Gly	Ser	Leu	Val	Glu	Ile	Ser	Gly	Gly	Met	Asp	Ile	Met	Glu	
		195					200					205				
Lys	Lys	Leu	Leu	Phe	Trp	Met	Ile	Phe	Met	Ala	Gly	Tyr	Leu	Gly	Met	
		210				215						220				
Ile	Tyr	Asp	Cys	Val	Thr	Gly	Ile	His	Leu	Arg	Leu	Lys	Gly	Val	Leu	
225					230					235					240	
Phe	Leu	Phe	Trp	Pro	Ala	Val	Phe	Leu	Pro	Ala	Ile	Arg	Pro	Pro	Arg	
				245					250					255		
Asn	Gly	Thr	Pro	Gln	Leu	Leu	Ser	Gln	Leu	Lys	Leu	Ser	Ile	Gly	Gly	
			260					265						270		

Leu Leu Leu Cys Asn Phe Gly Arg Leu Leu Glu Asn Asn Pro Arg Arg  
 275 280 285  
 Tyr Pro Lys Ala Asp Leu Lys Gln Trp Thr His Pro Val Pro Phe Ser  
 290 295 300  
 His Ile Lys Ile Thr Glu Ser Phe Leu Leu Ser His Arg Asn Gly Phe  
 305 310 315 320  
 Tyr Phe Tyr Ser Phe Arg Gly Ser Phe Arg Ile Asn Ser Leu Asn Cys  
 325 330 335  
 Thr Ile Val Asn Leu Thr Thr Phe Trp Ala Val Val Ala Phe Trp Ser  
 340 345 350  
 Ala Pro Arg Pro Val Cys Ser Thr Leu Val Trp Val Phe Lys Trp Ser  
 355 360 365  
 His Ser Trp Phe Leu Leu Leu Phe Gly Trp Asn Gln Ser Ile Val Trp  
 370 375 380  
 Ser Ser Ser Gly Leu Gly Val Lys Tyr Leu Glu Trp Val Lys Gly Cys  
 385 390 395 400  
 Leu Met Val Trp Arg Glu Glu Leu Ile Gly Ser Ala Lys Leu Val Glu  
 405 410 415  
 Gly Val Thr Lys Leu Ala Ser Lys Ile Thr Thr Val Asp Pro Thr Pro  
 420 425 430  
 Leu Leu Glu Val Met Gly Ser Leu Gly Asn Ser Tyr Leu Ala Phe Leu  
 435 440 445  
 Ile Arg Tyr Trp Lys Gly Arg Gly Arg Gly Leu Val Pro Pro Glu Gly  
 450 455 460  
 Gly Arg Asn Trp Pro Met Leu Asn Leu Ser Ser Leu Thr Phe Gln Asp  
 465 470 475 480  
 Gly Cys Glu Cys Pro Pro Leu Met Val Ser Thr Asn Ser Leu Glu Arg  
 485 490 495  
 Arg Glu Leu Lys Ile Pro Val Phe Arg Arg His Leu Arg Phe Leu Lys  
 500 505 510  
 Ala Gly Cys Thr Lys Tyr Gly Leu Leu Arg Arg Met Phe Pro Arg Trp  
 515 520 525  
 Leu Arg Gly Arg Val Arg Leu Leu Arg Arg Leu Leu Gly His Val Ile  
 530 535 540  
 Leu Lys Lys Lys Cys Ala Ala Val Val  
 545 550

<210> 5

<211> 1759

<212> DNA

<213> Type A PWD circovirus

<400> 5

aatactacag cagcgcactt ctttcacttt tataggatga cgtggccaag gaggcgttac	60
cgcagaagac ggacccgccc ccgcagccat cttggaaacg tcctccggag aagaccatat	120
ttggtacacc ccgccttcag aaaccgttac agatggcgcc gaaagacggg tatcttcaat	180
tcccgccttt ctagagaatt tgtactcacc ataagaggag gacactcgca gccatcttgg	240
aatgttaacg agctgagatt caacatcggc cagttcctcc cccctcagg cggcaccaac	300
cccctacccc tacctttcca atactaccgt attagaaagg ctaaatatga attttacccc	360
agagacccca tcacctctaa tcaaagaggt gttgggtcca ctgttggttat cttggatgcc	420
aactttgtaa cccctccac caacttggcc tatgaccctt atattaacta ctctcccg	480
cacaccataa ggcagccctt tacctaccac tccaggtact tcacccccaa accagagcta	540
gaccaaacia ttgattgggt ccagccaaat aataaaagaa accagctgtg gctccattta	600
aatacccaca ccaatgtcga gcacacaggc ctgggctatg cgctccaaaa tgcaaccaca	660
gcccataatt atgtggtaag gttgactatt tatgtacaat tcagagaatt tatcctgaaa	720
gacctctaa atgaataaaa ataaaaacca ttacgatgtg ataacaaaaa agactcagta	780
atttatttta tatgggaaaa gggcacaggg tgggtccact gcttcaaate ggccttcggg	840
tacctcgtg gattgttctc cagcagtctt ccaaaattgc aaagtagtaa tcctccgata	900
gagagcttct acagctggga cagcagttga ggagtaccat tcctgggggg cctgattgct	960
ggtaatcaaa atactgcggg ccaaaaaagg aacagtaccc cctttagtct ctacagtcaa	1020
tggataccgg tcacacagtc tcagtagatc atcccaaggt aaccagccat aaaaatcatc	1080
caaaacaaca acttcttctc catgatatcc atcccaccac ttatttctac taggcttcca	1140
gtaggtgtcc ctaggctcag caaaattacg ggccactgg ctcttccac aaccgggcgg	1200
gccactatg acgtgtacag ctgtcttcca atcacgtgc tgcattctcc cgctcacttt	1260
caaaagttca gccagcccg gcgaaattct cacatacgtt acaggaaact gctcggctac	1320

agtcacaaaa gaccccgctct ccaaaagggt actcacagca gtagacaggt cgctgcgctt 1380  
 cccctgggttc cgcgagctc cacactcgat aagtatgtgg ccttctttac tgcagtattc 1440  
 tttattctgc tggtcgggttc ctttcgcttt ctcgatgtgg cagcgggcac caaaatacca 1500  
 cttcaccttg ttaaaagtct gcttcttagc aaaattcgca aaccctgga ggtgaggagt 1560  
 tctacctctt tccaaacctt cctcgccaca aacaaaataa tcaaaaagggt agattggaag 1620  
 ctcccgattt ttgtttttct cctcctcgga aggattatta aggggaaca cccacctctt 1680  
 atgggggttc gggccgcttt tcttgcttgg cattttcact gacgctgccg aggtgctgcc 1740  
 gctgccgaag tgcgctggt 1759

<210> 6

<211> 567

<212> PRT

<213> Type A PWD circovirus

<400> 6

Gly	Ala	Cys	Lys	Pro	Leu	Pro	Leu	Val	Glu	Ala	Ala	Asp	Thr	Phe	Ile
1				5					10					15	
Gly	Leu	Leu	Phe	Leu	Pro	Gly	Cys	Gly	Trp	Leu	Leu	His	Thr	Asn	Val
			20					25					30		
Arg	Leu	Leu	Gly	Glu	Ser	Ser	Ser	Phe	Phe	Leu	Ile	Arg	Ser	Ser	Gly
		35					40					45			
Ile	Glu	Arg	Lys	Ser	Lys	Thr	Gln	Pro	Ser	Ser	Pro	Lys	Ser	Ser	Pro
	50					55					60				
Leu	Val	Gly	Arg	Trp	Pro	Asn	Ala	Phe	Lys	Ala	Leu	Phe	Cys	Val	Lys
65					70					75					80
Leu	Leu	Thr	Phe	His	Tyr	Lys	Pro	Ala	Arg	Gln	Trp	Met	Ser	Phe	Ala
				85					90					95	
Phe	Pro	Val	Ser	Trp	Cys	Phe	Leu	Ser	Tyr	Gln	Leu	Leu	Ser	Pro	Trp
		100						105					110		
Met	Ser	Ile	Ser	His	Pro	Ala	Gly	Arg	Phe	Trp	Pro	Phe	Arg	Leu	Ser
		115					120					125			
Arg	Asp	Val	Ala	Thr	Leu	Val	Arg	Lys	Ser	Val	Pro	Asp	Lys	Thr	Val
	130					135					140				

Thr	Ala	Ser	Cys	Asn	Gly	Thr	Val	Tyr	Thr	Leu	Phe	Lys	Arg	Pro	Ser	
145					150					155					160	
Ala	Ser	Ser	Lys	Phe	Thr	Leu	Pro	Phe	Ile	Cys	Cys	Arg	Ser	Gln	Phe	
				165					170					175		
Val	Ala	Thr	Cys	Thr	Met	Thr	Pro	Gly	Gly	Pro	Gln	Pro	Phe	Leu	Trp	
			180					185						190		
His	Ala	Arg	Leu	Lys	Ala	Ser	Gly	Leu	Ser	Val	Gln	Phe	Gly	Leu	Leu	
		195					200					205				
Phe	Leu	His	His	Ser	Pro	Tyr	Pro	Ser	Ser	Thr	Thr	Thr	Lys	Ser	Ser	
	210					215						220				
Lys	Pro	Gln	Asn	Gly	Gln	Ser	Ser	Arg	Ser	Leu	Ser	His	Ser	Arg	Tyr	
225					230					235					240	
Gly	Asn	Val	Thr	Ser	Val	Leu	Pro	Pro	Val	Thr	Gly	Lys	Lys	Ala	Arg	
				245					250					255		
Leu	Ile	Lys	Ile	Val	Leu	Leu	Ala	Gly	Trp	Ser	His	Tyr	Glu	Glu	Val	
		260						265					270			
Ala	Thr	Gly	Ala	Thr	Ser	Ala	Arg	Arg	Leu	Ile	Val	Val	Lys	Cys	Asn	
		275					280					285				
Gln	Phe	Val	Ala	Pro	Ser	Cys	Asp	Val	Ser	Thr	Gly	Ser	Pro	Arg	Asn	
	290					295					300					
Ser	Ala	Thr	Ser	Gly	Gly	Gln	Ala	Arg	Lys	Gly	Tyr	Leu	Ile	Phe	Gln	
305					310					315					320	
Thr	Lys	Lys	Thr	Ile	Val	Asp	Tyr	His	Asn	Lys	Asn	Lys	Asn	Met	Leu	
				325					330					335		
Thr	Lys	Ser	Leu	Asn	Glu	Ser	Asn	Tyr	Met	Phe	Leu	Gly	Trp	Met	Ile	
			340					345					350			
Lys	Pro	Gln	Pro	Gln	Met	Lys	Ser	Arg	Met	Ala	Trp	Ala	Gln	Thr	Ser	
		355					360					365				
Ser	Met	Pro	Thr	Pro	Ile	Ile	Ser	Gly	Cys	Ser	Thr	Glu	Lys	Ile	Ile	
	370					375					380					
Gln	Ser	Ser	Gly	Ile	Leu	Gln	Lys	Thr	Ser	Gln	Asn	Pro	Pro	Ser	Thr	
385					390					395					400	
Gly	Pro	Thr	Thr	Pro	Leu	Pro	Ser	Gly	Pro	Thr	Ala	Pro	Pro	Thr	Thr	
				405					410					415		
Leu	Ile	Pro	Thr	Met	Pro	Trp	Thr	Pro	Pro	Pro	Pro	Leu	Thr	Pro	Met	
			420					425					430			



Trp Ser Leu Leu Leu Pro Gly Leu Val Glu Lys Ile Leu Pro Ser Pro  
 435 440 445

Thr Glu Pro Thr Phe Asn Met Asn Leu Arg Glu Leu Val Thr Thr Asn  
 450 455 460

Ser Leu Tyr Pro Tyr Pro Thr Pro Ala Ala Gln Pro Pro Ser Ser Ser  
 465 470 475 480

Ala Ser Thr Ser Asp Ser Thr Leu Met Gly Leu His Ser Arg Thr Asp  
 485 490 495

Glu Glu Pro Ser Tyr Leu Asn Glu Leu Phe Ala Pro Ile Ser Ser Val  
 500 505 510

Arg Arg Glu Ala Gly Asp Thr Val Thr Glu Ser Pro Pro Thr Tyr Trp  
 515 520 525

Ile His Asp Glu Gly Ser Ser Thr Glu Leu Ile Ala Ala Pro Ala Pro  
 530 535 540

Gly Asp Glu Ala Thr Val Gly Gly Gln Gly Arg Gly Ile Phe Thr Phe  
 545 550 555 560

Ser Thr Arg Gln Gln Leu Ile  
 565

<210> 7

<211> 580

<212> PRT

<213> Type A PWD circovirus

<400> 7

Trp Arg Val Glu Ala Ala Ala Ala Gly Arg Cys Arg His Phe His Trp  
 1 5 10 15

Ala Leu Phe Ala Ala Arg Leu Gly Met Leu Pro Pro His Glu Gly Lys  
 20 25 30

Ile Ile Arg Gly Leu Leu Leu Phe Val Phe Tyr Pro Leu Lys Trp Asp  
 35 40 45

Gly Lys Lys Ile Ile Lys Asn Thr Ala Leu Phe Thr Gln Phe Leu Thr  
 50 55 60

Ser Ser Arg Val Glu Leu Pro Lys Arg Ile Lys Ser Leu Leu Leu Ser  
 65 70 75 80

Lys Val Leu His Leu Pro Ile Lys Thr Gly Ala Ala Val Asp Leu Phe  
 85 90 95  
 Arg Phe Ser Gly Val Leu Leu Ile Phe Phe Val Ala Thr Phe Phe Ala  
 100 105 110  
 Val Tyr Lys Asp Leu Thr Ser Ser Arg Pro Val Leu Pro Leu Ala Ala  
 115 120 125  
 Val Gln Arg Ser Ser His Thr Gly Lys Gln Leu Arg Pro Arg Gln His  
 130 135 140  
 Ser Tyr Gly Leu Leu Lys Arg Tyr Arg Ile His Ser Ile Glu Ala Pro  
 145 150 155 160  
 Gln Ser Phe Lys Gln Phe His Ala Pro Leu His Leu Leu Thr Ile Pro  
 165 170 175  
 Leu Cys Ser Tyr Val Asp Tyr His Ala Arg Gly Thr Thr Pro Leu Ala  
 180 185 190  
 Leu Pro Gly Thr Ile Lys Ser Leu Arg Pro Val Gly Val Pro Leu Arg  
 195 200 205  
 Thr Ser Ile Leu Pro Pro Ile Ser Ile Met Ser Phe Phe Asn Asn Asn  
 210 215 220  
 Gln Ile Ile Lys Ile Ala Pro Arg Pro Ile Ile Gln Ser Gln Thr Val  
 225 230 235 240  
 Pro Ile Trp Gln Ser Tyr Leu Ser Phe Pro Thr Ser Asn Arg Lys Gln  
 245 250 255  
 Gly Ala Thr Asn Gln Asn Gly Ala Ile Leu Gly Gly Leu Phe Pro Val  
 260 265 270  
 Gly Ser Ser Asp Trp Ser Tyr Phe Ser Glu Ile Pro Pro Asn Ser Ser  
 275 280 285  
 Gln Leu Lys Pro Leu Ser Ser Ser Phe Leu Gly Arg Leu Tyr Gly Phe  
 290 295 300  
 Ala Ser Lys Phe Cys His Val Trp Gly Thr Gly Lys Glu Trp Ile Phe  
 305 310 315 320  
 Tyr Ile Val Ser Asp Lys Lys Asn Asp Cys Arg Leu Pro Lys Lys Glu  
 325 330 335  
 Asn Leu Pro Asp Lys Leu Ile Phe Glu Arg Phe Gln Val Tyr Ile Thr  
 340 345 350  
 Leu Arg Val Val Tyr Asn Gln Ala Thr Thr Ala Asn Gln Leu Ala Tyr  
 355 360 365

103

Gly Leu Gly Thr His Glu Val Asn Thr His Thr Asn Leu His Leu Trp  
370 375 380

Leu Gln Asn Arg Lys Asn Asn Pro Gln Phe Trp Asp Ile Thr Gln Asp  
385 390 395 400

Leu Glu Pro Lys Pro Thr Phe Tyr Arg Ser His Tyr Thr Phe Pro Gln  
405 410 415

Arg Ile Thr His Arg Ser Ser Tyr Asn Ile His Pro Asp Tyr Ala Leu  
420 425 430

Asn Thr Ser Pro Thr Val Phe Asn Ala Asp Leu Ile Val Val Thr Ser  
435 440 445

Gly Val Gly Arg Gln Asn Ser Thr Ile Pro Asp Arg Pro Tyr Phe Glu  
450 455 460

Tyr Lys Ala Lys Arg Ile Arg Tyr Tyr Gln Phe Pro Leu Pro Leu Pro  
465 470 475 480

Asn Thr Gly Gly Ser Pro Pro Leu Phe Gln Gly Ile Asn Phe Arg Leu  
485 490 495

Glu Asn Val Asn Trp Ser Pro Gln Ser His Gly Gly Arg Ile Thr Leu  
500 505 510

Val Phe Glu Arg Ser Leu Arg Ser Asn Phe Ile Gly Thr Lys Arg Arg  
515 520 525

Trp Arg Tyr Arg Asn Arg Phe Ala Pro His Val Leu Tyr Pro Arg Arg  
530 535 540

Arg Leu Ile Asn Gly Leu His Ser Arg Pro Arg Thr Arg Arg Arg Arg  
545 550 555 560

Tyr Arg Arg Arg Pro Trp Thr Met Arg Tyr Phe His Phe Phe His Ala  
565 570 575

Ala Thr Thr Asn  
580

<210> 8

<211> 557

<212> PRT

<213> Type A PWD circovirus

<400> 8

Leu	Ala	Ser	Arg	Cys	Arg	Cys	Cys	Arg	Pro	Leu	Thr	Leu	Ser	Phe	Ala	
1				5					10					15		
Leu	Cys	Ser	Phe	Arg	Gly	Ala	Val	Gly	Tyr	Ser	Thr	Pro	Thr	Gly	Tyr	
			20					25					30			
Asp	Lys	Arg	Pro	Pro	Ser	Phe	Cys	Phe	Val	Pro	Ala	Glu	Leu	Arg	Gly	
	35						40					45				
Lys	Gln	Asn	Asn	Gln	Lys	His	Arg	Pro	Leu	Asn	Pro	Leu	Pro	Tyr	Phe	
	50					55					60					
Glu	Glu	Gly	Gly	Pro	Thr	Gln	Ser	Asn	Gln	Ser	Ala	Ser	Lys	Cys	Pro	
65					70				75						80	
Ser	Thr	Thr	Asn	Gly	His	Gly	Ser	Gly	Cys	Arg	Ser	Leu	Ser	Leu	Phe	
			85						90					95		
Arg	Gly	Ala	Ser	Tyr	Leu	Ile	Ser	Cys	Tyr	Leu	Leu	Gly	Cys	Val	Arg	
			100					105					110			
Thr	His	Leu	Glu	Ala	Ser	Gly	Pro	Ser	Ala	Cys	Arg	Gly	Thr	Gln	Gln	
	115						120					125				
Ser	Tyr	Gly	Lys	Pro	Ser	Pro	Thr	Lys	Pro	Ser	Gln	Leu	Arg	Ala	Thr	
	130					135					140					
Glu	Gln	Leu	Thr	His	Ser	Phe	Asn	Gly	Arg	Ala	Pro	Gln	Val	Lys	Ser	
145					150				155						160	
Leu	Ser	Arg	Ser	Ser	Ala	Ala	Ala	His	Asn	Ser	Ser	Leu	Gln	Val	Arg	
				165					170					175		
Leu	Pro	Gly	Ala	Arg	Asn	His	Ser	Ser	Gly	Thr	Pro	Gly	Tyr	Asn	Gln	
		180						185					190			
Gln	Ala	Pro	Cys	Arg	Ser	Ser	Ala	Tyr	Phe	Tyr	Thr	Thr	Pro	His	Ile	
	195						200					205				
Asp	His	Leu	Leu	Leu	Gln	Gln	Lys	Pro	His	Asn	Lys	His	Ser	Thr	Val	
	210					215					220					
Lys	Pro	His	Asp	Val	Ser	Val	Thr	His	Gly	Thr	Asp	Met	Ser	Gln	Leu	
225					230					235					240	
Ser	Leu	Pro	Tyr	Gln	Glu	Lys	Lys	Pro	Gly	Cys	Tyr	Lys	Ser	Trp	Cys	
				245					250					255		
Asp	Pro	Gly	Gly	Pro	Ile	Thr	Ser	Arg	Leu	Gln	Gln	Gly	Leu	Gln	Leu	
		260					265						270			
Leu	Glu	Arg	Asp	Ser	Ser	Lys	Ala	Ile	Lys	Ser	Ser	Gln	Gln	Leu	Val	
	275						280					285				

105

Ile Trp Pro Pro Val Arg Leu Gly Ile Gln Leu Leu Pro Gly Val Arg  
290 295 300

His Gly Lys Gly Met Tyr Phe Leu Asn Ser Leu Arg Lys Gln Met Thr  
305 310 315 320

Ile Thr Lys Ile Lys Ile Lys Ser Pro Arg Glu Pro Tyr Ile Arg Gln  
325 330 335

Ile Thr Cys Leu Tyr Asp Val Lys Gly Cys Leu Lys Pro Ser His Asn  
340 345 350

Cys Lys Pro Ala Cys Leu Gly Pro Arg His Ala Arg Cys Gln His Pro  
355 360 365

Tyr Lys Phe Pro Ala Val Val Pro Lys Lys Lys Ala Pro Val Leu Asn  
370 375 380

Asn Pro Arg Ala Arg Thr Gln Pro His Leu Val Gln Leu Pro Leu Tyr  
385 390 395 400

Leu Ala Ala Lys His His Pro Pro Leu Leu Leu Tyr Leu Pro Leu Gly  
405 410 415

Leu Gln His Leu Pro Asn Cys Leu Gln Cys Gly Leu Tyr Cys Cys His  
420 425 430

Val Trp Cys Arg Lys Ser Leu His His Pro Arg Gln Pro Leu Ile Ile  
435 440 445

Gly Lys Tyr Pro Leu Ile Pro Phe Thr Pro Thr Pro Pro Gln His Arg  
450 455 460

Arg Leu Pro Pro Pro Val Pro Arg His Gln Ile Glu Ala Arg Cys Glu  
465 470 475 480

Leu Ile Ala Ala Leu Thr Arg Arg Lys His His Thr Cys Ile Arg Phe  
485 490 495

Pro Pro Phe Gln Leu Tyr Gly Asp Lys Pro Ala Met Gln Leu Pro Lys  
500 505 510

Gln Leu Arg Pro Thr Gly Phe Ile Thr Lys Glu Pro Pro His Lys Trp  
515 520 525

Ser Pro Gln Pro Pro Pro Asp Thr Lys Gln Pro Leu Ala Glu Lys Ala  
530 535 540

Val Asp Asp Leu Leu Ser Leu Leu Ala Ser Ser Tyr Tyr  
545 550 555

<210> 9

<211> 939

<212> DNA

<213> Type A PWD circovirus

<220>

<221> CDS

<222> (1)..(936)

<400> 9

atg cca agc aag aaa agc ggc ccg caa ccc cat aag agg tgg gtg ttc	48
Met Pro Ser Lys Lys Ser Gly Pro Gln Pro His Lys Arg Trp Val Phe	
1 5 10 15	
acc ctt aat aat cct tcc gag gag gag aaa aac aaa ata cgg gag ctt	96
Thr Leu Asn Asn Pro Ser Glu Glu Glu Lys Asn Lys Ile Arg Glu Leu	
20 25 30	
cca atc tcc ctt ttt gat tat ttt gtt tgt ggc gag gaa ggt ttg gaa	144
Pro Ile Ser Leu Phe Asp Tyr Phe Val Cys Gly Glu Glu Gly Leu Glu	
35 40 45	
gag ggt aga act cct cac ctc cag ggg ttt gcg aat ttt gct aag aag	192
Glu Gly Arg Thr Pro His Leu Gln Gly Phe Ala Asn Phe Ala Lys Lys	
50 55 60	
cag act ttt aac aag gtg aag tgg tat ttt ggt gcc cgc tgc cac atc	240
Gln Thr Phe Asn Lys Val Lys Trp Tyr Phe Gly Ala Arg Cys His Ile	
65 70 75 80	
gag aaa gcg aaa gga acc gac cag cag aat aaa gaa tac tgc agt aaa	288
Glu Lys Ala Lys Gly Thr Asp Gln Gln Asn Lys Glu Tyr Cys Ser Lys	
85 90 95	
gaa ggc cac ata ctt atc gag tgt gga gct ccg cgg aac cag ggg aag	336
Glu Gly His Ile Leu Ile Glu Cys Gly Ala Pro Arg Asn Gln Gly Lys	
100 105 110	
cgc agc gac ctg tct act gct gtg agt acc ctt ttg gag acg ggg tct	384
Arg Ser Asp Leu Ser Thr Ala Val Ser Thr Leu Leu Glu Thr Gly Ser	
115 120 125	
ttg gtg act gta gcc gag cag ttt cct gta acg tat gtg aga aat ttc	432
Leu Val Thr Val Ala Glu Gln Phe Pro Val Thr Tyr Val Arg Asn Phe	
130 135 140	
cgc ggg ctg gct gaa ctt ttg aaa gtg agc ggg aag atg cag cag cgt	480
Arg Gly Leu Ala Glu Leu Leu Lys Val Ser Gly Lys Met Gln Gln Arg	
145 150 155 160	

gat	tgg	aag	aca	gct	gta	cac	gtc	ata	gtg	ggc	ccg	ccc	ggg	tgt	ggg	528
Asp	Trp	Lys	Thr	Ala	Val	His	Val	Ile	Val	Gly	Pro	Pro	Gly	Cys	Gly	
				165					170					175		

aag	agc	cag	tgg	gcc	cgt	aat	ttt	gct	gag	cct	agg	gac	acc	tac	tgg	576
Lys	Ser	Gln	Trp	Ala	Arg	Asn	Phe	Ala	Glu	Pro	Arg	Asp	Thr	Tyr	Trp	
			180					185					190			

aag	cct	agt	aga	aat	aag	tgg	tgg	gat	gga	tat	cat	gga	gaa	gaa	gtt	624
Lys	Pro	Ser	Arg	Asn	Lys	Trp	Trp	Asp	Gly	Tyr	His	Gly	Glu	Glu	Val	
		195					200					205				

gtt	gtt	ttg	gat	gat	ttt	tat	ggc	tgg	tta	cct	tgg	gat	gat	cta	ctg	672
Val	Val	Leu	Asp	Asp	Phe	Tyr	Gly	Trp	Leu	Pro	Trp	Asp	Asp	Leu	Leu	
	210					215					220					

aga	ctg	tgt	gac	cgg	tat	cca	ttg	act	gta	gag	act	aaa	ggg	ggg	act	720
Arg	Leu	Cys	Asp	Arg	Tyr	Pro	Leu	Thr	Val	Glu	Thr	Lys	Gly	Gly	Thr	
	225				230					235					240	

gtt	cct	ttt	ttg	gcc	cgc	agt	att	ttg	att	acc	agc	aat	cag	gcc	ccc	768
Val	Pro	Phe	Leu	Ala	Arg	Ser	Ile	Leu	Ile	Thr	Ser	Asn	Gln	Ala	Pro	
				245					250					255		

cag	gaa	tgg	tac	tcc	tca	act	gct	gtc	cca	gct	gta	gaa	gct	ctc	tat	816
Gln	Glu	Trp	Tyr	Ser	Ser	Thr	Ala	Val	Pro	Ala	Val	Glu	Ala	Leu	Tyr	
			260					265					270			

cgg	agg	att	act	act	ttg	caa	ttt	tgg	aag	act	gct	gga	gaa	caa	tcc	864
Arg	Arg	Ile	Thr	Thr	Leu	Gln	Phe	Trp	Lys	Thr	Ala	Gly	Glu	Gln	Ser	
		275					280					285				

acg	gag	gta	ccc	gaa	ggc	cga	ttt	gaa	gca	gtg	gac	cca	ccc	tgt	gcc	912
Thr	Glu	Val	Pro	Glu	Gly	Arg	Phe	Glu	Ala	Val	Asp	Pro	Pro	Cys	Ala	
	290					295					300					

ctt	ttc	cca	tat	aaa	ata	aat	tac	tga								939
Leu	Phe	Pro	Tyr	Lys	Ile	Asn	Tyr									
305					310											

<210> 10

<211> 312

<212> PRT

<213> Type A PWD circovirus

<400> 10

Met	Pro	Ser	Lys	Lys	Ser	Gly	Pro	Gln	Pro	His	Lys	Arg	Trp	Val	Phe	
1				5					10					15		

Thr Leu Asn Asn Pro Ser Glu Glu Glu Lys Asn Lys Ile Arg Glu Leu  
 20 25 30

Pro Ile Ser Leu Phe Asp Tyr Phe Val Cys Gly Glu Glu Gly Leu Glu  
 35 40 45

Glu Gly Arg Thr Pro His Leu Gln Gly Phe Ala Asn Phe Ala Lys Lys  
 50 55 60

Gln Thr Phe Asn Lys Val Lys Trp Tyr Phe Gly Ala Arg Cys His Ile  
 65 70 75 80

Glu Lys Ala Lys Gly Thr Asp Gln Gln Asn Lys Glu Tyr Cys Ser Lys  
 85 90 95

Glu Gly His Ile Leu Ile Glu Cys Gly Ala Pro Arg Asn Gln Gly Lys  
 100 105 110

Arg Ser Asp Leu Ser Thr Ala Val Ser Thr Leu Leu Glu Thr Gly Ser  
 115 120 125

Leu Val Thr Val Ala Glu Gln Phe Pro Val Thr Tyr Val Arg Asn Phe  
 130 135 140

Arg Gly Leu Ala Glu Leu Leu Lys Val Ser Gly Lys Met Gln Gln Arg  
 145 150 155 160

Asp Trp Lys Thr Ala Val His Val Ile Val Gly Pro Pro Gly Cys Gly  
 165 170 175

Lys Ser Gln Trp Ala Arg Asn Phe Ala Glu Pro Arg Asp Thr Tyr Trp  
 180 185 190

Lys Pro Ser Arg Asn Lys Trp Trp Asp Gly Tyr His Gly Glu Glu Val  
 195 200 205

Val Val Leu Asp Asp Phe Tyr Gly Trp Leu Pro Trp Asp Asp Leu Leu  
 210 215 220

109



Arg Leu Cys Asp Arg Tyr Pro Leu Thr Val Glu Thr Lys Gly Gly Thr  
225 230 235 240

Val Pro Phe Leu Ala Arg Ser Ile Leu Ile Thr Ser Asn Gln Ala Pro  
245 250 255

Gln Glu Trp Tyr Ser Ser Thr Ala Val Pro Ala Val Glu Ala Leu Tyr  
260 265 270

Arg Arg Ile Thr Thr Leu Gln Phe Trp Lys Thr Ala Gly Glu Gln Ser  
275 280 285

Thr Glu Val Pro Glu Gly Arg Phe Glu Ala Val Asp Pro Pro Cys Ala  
290 295 300

Leu Phe Pro Tyr Lys Ile Asn Tyr  
305 310

<210> 11

<211> 702

<212> DNA

<213> Type A PWD circovirus

<220>

<221> CDS

<222> (1) ... (699)

<400> 11

atg acg tgg cca agg agg cgt tac cgc aga aga cgg acc cgc ccc cgc 48  
Met Thr Trp Pro Arg Arg Arg Tyr Arg Arg Arg Arg Thr Arg Pro Arg  
1 5 10 15

agc cat ctt gga aac atc ctc cgg aga aga cca tat ttg gta cac ccc 96  
Ser His Leu Gly Asn Ile Leu Arg Arg Arg Pro Tyr Leu Val His Pro  
20 25 30

gcc ttc aga aac cgt tac aga tgg cgc cga aag acg ggt atc ttc aat 144  
Ala Phe Arg Asn Arg Tyr Arg Trp Arg Arg Lys Thr Gly Ile Phe Asn  
35 40 45

tcc cgc ctt tct aga gaa ttt gta ctc acc ata aga gga gga cac tcg Ser Arg Leu Ser Arg Glu Phe Val Leu Thr Ile Arg Gly Gly His Ser 50 55 60	192
cag cca tct tgg aat gtt aac gag ctg aga ttc aac atc ggc cag ttc Gln Pro Ser Trp Asn Val Asn Glu Leu Arg Phe Asn Ile Gly Gln Phe 65 70 75 80	240
ctc ccc ccc tca ggc ggc acc aac ccc cta ccc cta cct ttc caa tac Leu Pro Pro Ser Gly Gly Thr Asn Pro Leu Pro Leu Pro Phe Gln Tyr 85 90 95	288
tac cgt att aga aag gct aaa tat gaa ttt tac ccc aga gac ccc atc Tyr Arg Ile Arg Lys Ala Lys Tyr Glu Phe Tyr Pro Arg Asp Pro Ile 100 105 110	336
acc tct aat caa aga ggt gtt ggg tcc act gtt gtt atc ttg gat gcc Thr Ser Asn Gln Arg Gly Val Gly Ser Thr Val Val Ile Leu Asp Ala 115 120 125	384
aac ttt gta acc ccc tcc acc aac ttg gcc tat gac ccc tat att aac Asn Phe Val Thr Pro Ser Thr Asn Leu Ala Tyr Asp Pro Tyr Ile Asn 130 135 140	432
tac tcc tcc cgc cac acc ata agg cag ccc ttt acc tac cac tcc agg Tyr Ser Ser Arg His Thr Ile Arg Gln Pro Phe Thr Tyr His Ser Arg 145 150 155 160	480
tac ttc acc ccc aaa cca gag cta gac caa aca att gat tgg ttc cag Tyr Phe Thr Pro Lys Pro Glu Leu Asp Gln Thr Ile Asp Trp Phe Gln 165 170 175	528
cca aat aat aaa aga aac cag ctg tgg ctc cat tta aat acc cac acc Pro Asn Asn Lys Arg Asn Gln Leu Trp Leu His Leu Asn Thr His Thr 180 185 190	576
aat gtc gag cac aca ggc ctg ggc tat gcg ctc caa aat gca acc aca Asn Val Glu His Thr Gly Leu Gly Tyr Ala Leu Gln Asn Ala Thr Thr 195 200 205	624
gcc caa aat tat gtg gta agg ttg act att tat gta caa ttc aga gaa Ala Gln Asn Tyr Val Val Arg Leu Thr Ile Tyr Val Gln Phe Arg Glu 210 215 220	672
ttt atc ctg aaa gac cct cta aat gaa taa Phe Ile Leu Lys Asp Pro Leu Asn Glu 225 230	702

<210> 12

<211> 233

<212> PRT

<213> Type A PWD circovirus

<400> 12

Met Thr Trp Pro Arg Arg Arg Tyr Arg Arg Arg Arg Thr Arg Pro Arg  
1 5 10 15

Ser His Leu Gly Asn Ile Leu Arg Arg Arg Pro Tyr Leu Val His Pro  
20 25 30

Ala Phe Arg Asn Arg Tyr Arg Trp Arg Arg Lys Thr Gly Ile Phe Asn  
35 40 45

Ser Arg Leu Ser Arg Glu Phe Val Leu Thr Ile Arg Gly Gly His Ser  
50 55 60

Gln Pro Ser Trp Asn Val Asn Glu Leu Arg Phe Asn Ile Gly Gln Phe  
65 70 75 80

Leu Pro Pro Ser Gly Gly Thr Asn Pro Leu Pro Leu Pro Phe Gln Tyr  
85 90 95

Tyr Arg Ile Arg Lys Ala Lys Tyr Glu Phe Tyr Pro Arg Asp Pro Ile  
100 105 110

Thr Ser Asn Gln Arg Gly Val Gly Ser Thr Val Val Ile Leu Asp Ala  
115 120 125

Asn Phe Val Thr Pro Ser Thr Asn Leu Ala Tyr Asp Pro Tyr Ile Asn  
130 135 140

Tyr Ser Ser Arg His Thr Ile Arg Gln Pro Phe Thr Tyr His Ser Arg  
145 150 155 160

Tyr Phe Thr Pro Lys Pro Glu Leu Asp Gln Thr Ile Asp Trp Phe Gln  
165 170 175

Pro Asn Asn Lys Arg Asn Gln Leu Trp Leu His Leu Asn Thr His Thr  
180 185 190

Asn Val Glu His Thr Gly Leu Gly Tyr Ala Leu Gln Asn Ala Thr Thr  
 195 200 205

Ala Gln Asn Tyr Val Val Arg Leu Thr Ile Tyr Val Gln Phe Arg Glu  
 210 215 220

Phe Ile Leu Lys Asp Pro Leu Asn Glu  
 225 230

<210> 13

<211> 621

<212> DNA

<213> Type A PWD circovirus

<220>

<221> CDS

<222> (1)..(618)

<400> 13

atg	ata	tcc	atc	cca	cca	ctt	att	tct	act	agg	ctt	cca	gta	ggt	gtc	48
Met	Ile	Ser	Ile	Pro	Pro	Leu	Ile	Ser	Thr	Arg	Leu	Pro	Val	Gly	Val	
1				5					10					15		

cct	agg	ctc	agc	aaa	att	acg	ggc	cca	ctg	gct	ctt	ccc	aca	acc	ggg	96
Pro	Arg	Leu	Ser	Lys	Ile	Thr	Gly	Pro	Leu	Ala	Leu	Pro	Thr	Thr	Gly	
			20					25					30			

cgg	gcc	cac	tat	gac	gtg	tac	agc	tgt	ctt	cca	atc	acg	ctg	ctg	cat	144
Arg	Ala	His	Tyr	Asp	Val	Tyr	Ser	Cys	Leu	Pro	Ile	Thr	Leu	Leu	His	
		35					40						45			

ctt	ccc	gct	cac	ttt	caa	aag	ttc	agc	cag	ccc	gcg	gaa	att	tct	cac	192
Leu	Pro	Ala	His	Phe	Gln	Lys	Phe	Ser	Gln	Pro	Ala	Glu	Ile	Ser	His	
	50					55					60					

ata	cgt	tac	agg	aaa	ctg	ctc	ggc	tac	agt	cac	caa	aga	ccc	cgt	ctc	240
Ile	Arg	Tyr	Arg	Lys	Leu	Leu	Gly	Tyr	Ser	His	Gln	Arg	Pro	Arg	Leu	
65					70				75					80		

caa	aag	ggt	act	cac	agc	agt	aga	cag	gtc	gct	gcg	ctt	ccc	ctg	gtt	288
Gln	Lys	Gly	Thr	His	Ser	Ser	Arg	Gln	Val	Ala	Ala	Leu	Pro	Leu	Val	
				85					90					95		

ccg cgg agc tcc aca ctc gat aag tat gtg gcc ttc ttt act gca gta 336  
 Pro Arg Ser Ser Thr Leu Asp Lys Tyr Val Ala Phe Phe Thr Ala Val  
                   100                                  105                                  110

ttc ttt att ctg ctg gtc ggt tcc ttt cgc ttt ctc gat gtg gca gcg 384  
 Phe Phe Ile Leu Leu Val Gly Ser Phe Arg Phe Leu Asp Val Ala Ala  
                   115                                  120                                  125

ggc acc aaa ata cca ctt cac ctt gtt aaa agt ctg ctt ctt agc aaa 432  
 Gly Thr Lys Ile Pro Leu His Leu Val Lys Ser Leu Leu Leu Ser Lys  
                   130                                  135                                  140

att cgc aaa ccc ctg gag gtg agg agt tct acc ctc ttc caa acc ttc 480  
 Ile Arg Lys Pro Leu Glu Val Arg Ser Ser Thr Leu Phe Gln Thr Phe  
 145                                  150                                  155                                  160

ctc gcc aca aac aaa ata atc aaa aag gga gat tgg aag ctc ccg tat 528  
 Leu Ala Thr Asn Lys Ile Ile Lys Lys Gly Asp Trp Lys Leu Pro Tyr  
                                   165                                  170                                  175

ttt gtt ttt ctc ctc ctc gga agg att att aag ggt gaa cac cca cct 576  
 Phe Val Phe Leu Leu Leu Gly Arg Ile Ile Lys Gly Glu His Pro Pro  
                   180                                  185                                  190

ctt atg ggg ttg cgg gcc gct ttt ctt gct tgg cat ttt cac tga 621  
 Leu Met Gly Leu Arg Ala Ala Phe Leu Ala Trp His Phe His  
                   195                                  200                                  205

<210> 14

<211> 206

<212> PRT

<213> Type A PWD circovirus

<400> 14

Met Ile Ser Ile Pro Pro Leu Ile Ser Thr Arg Leu Pro Val Gly Val  
 1                                  5                                  10                                  15

Pro Arg Leu Ser Lys Ile Thr Gly Pro Leu Ala Leu Pro Thr Thr Gly  
                   20                                  25                                  30

Arg Ala His Tyr Asp Val Tyr Ser Cys Leu Pro Ile Thr Leu Leu His  
                   35                                  40                                  45

Leu Pro Ala His Phe Gln Lys Phe Ser Gln Pro Ala Glu Ile Ser His  
                   50                                  55                                  60

Ile Arg Tyr Arg Lys Leu Leu Gly Tyr Ser His Gln Arg Pro Arg Leu  
65 70 75 80

Gln Lys Gly Thr His Ser Ser Arg Gln Val Ala Ala Leu Pro Leu Val  
85 90 95

Pro Arg Ser Ser Thr Leu Asp Lys Tyr Val Ala Phe Phe Thr Ala Val  
100 105 110

Phe Phe Ile Leu Leu Val Gly Ser Phe Arg Phe Leu Asp Val Ala Ala  
115 120 125

Gly Thr Lys Ile Pro Leu His Leu Val Lys Ser Leu Leu Leu Ser Lys  
130 135 140

Ile Arg Lys Pro Leu Glu Val Arg Ser Ser Thr Leu Phe Gln Thr Phe  
145 150 155 160

Leu Ala Thr Asn Lys Ile Ile Lys Lys Gly Asp Trp Lys Leu Pro Tyr  
165 170 175

Phe Val Phe Leu Leu Leu Gly Arg Ile Ile Lys Gly Glu His Pro Pro  
180 185 190

Leu Met Gly Leu Arg Ala Ala Phe Leu Ala Trp His Phe His  
195 200 205

<210> 15

<211> 1767

<212> DNA

<213> Type B PWD circovirus

<220>

<221> CDS

<222> (1)..(111)

115

<220>

<221> CDS

<222> (115) .. (243)

<220>

<221> CDS

<222> (247) .. (267)

<220>

<221> CDS

<222> (271) .. (360)

<220>

<221> CDS

<222> (364) .. (417)

<220>

<221> CDS

<222> (421) .. (447)

<220>

<221> CDS

<222> (451) .. (471)

<220>

<221> CDS

<222> (475) .. (510)

<220>

<221> CDS

<222> (514) .. (516)

<220>

<221> CDS

<222> (520) .. (729)

<220>

<221> CDS

<222> (733) .. (753)

<220>

<221> CDS

<222> (757) .. (759)

<220>

<221> CDS

<222> (763) .. (804)

<220>

<221> CDS

<222> (808) .. (861)

<220>

<221> CDS

<222> (865) .. (984)



<220>

<221> CDS

<222> (988)..(1173)

<220>

<221> CDS

<222> (1177)..(1233)

<220>

<221> CDS

<222> (1237)..(1359)

<220>

<221> CDS

<222> (1363)..(1476)

<220>

<221> CDS

<222> (1480)..(1737)

<220>

<221> CDS

<222> (1741)..(1767)

<400> 15

acc agc gca ctt cgg cag cgg cag cac ctc ggc agc acc tca gca gca  
Thr Ser Ala Leu Arg Gln Arg Gln His Leu Gly Ser Thr Ser Ala Ala  
1 5 10 15

48

aca tgc cca gca aga aga atg gaa gaa gcg gac ccc aac ccc ata aaa	96
Thr Cys Pro Ala Arg Arg Met Glu Glu Ala Asp Pro Asn Pro Ile Lys	
20 25 30	
ggt ggg tgt tca ctc tga ata atc ctt ccg aag acg agc gca aga aaa	144
Gly Gly Cys Ser Leu Ile Ile Leu Pro Lys Thr Ser Ala Arg Lys	
35 40 45	
tac ggg atc ttc caa tat ccc tat ttg att att tta ttg ttg gcg agg	192
Tyr Gly Ile Phe Gln Tyr Pro Tyr Leu Ile Ile Leu Leu Leu Ala Arg	
50 55 60	
agg gta atg agg aag gac gaa cac ctc acc tcc agg ggt tcg cta att	240
Arg Val Met Arg Lys Asp Glu His Leu Thr Ser Arg Gly Ser Leu Ile	
65 70 75	
ttg tga aga agc aga ctt tta ata aag tga agt ggt att tgg gtg ccc	288
Leu Arg Ser Arg Leu Leu Ile Lys Ser Gly Ile Trp Val Pro	
80 85 90	
gct gcc aca tcg aga aag cga aag gaa cag atc agc aga ata aag aat	336
Ala Ala Thr Ser Arg Lys Arg Lys Glu Gln Ile Ser Arg Ile Lys Asn	
95 100 105	
act gca gta aag aag gca act tac tga tgg agt gtg gag ctc cta gat	384
Thr Ala Val Lys Lys Ala Thr Tyr Trp Ser Val Glu Leu Leu Asp	
110 115 120	
ctc agg gac aac gga gtg acc tgt cta ctg ctg tga gta cct tgt tgg	432
Leu Arg Asp Asn Gly Val Thr Cys Leu Leu Leu Val Pro Cys Trp	
125 130 135	
aga gcg gga gtc tgg tga ccg ttg cag agc agc acc ctg taa cgt ttg	480
Arg Ala Gly Val Trp Pro Leu Gln Ser Ser Thr Leu Arg Leu	
140 145 150	
tca gaa att tcc gcg ggc tgg ctg aac ttt tga aag tga gcg gga aaa	528
Ser Glu Ile Ser Ala Gly Trp Leu Asn Phe Lys Ala Gly Lys	
155 160 165	
tgc aga agc gtg att gga aga cta atg tac acg tca ttg tgg ggc cac	576
Cys Arg Ser Val Ile Gly Arg Leu Met Tyr Thr Ser Leu Trp Gly His	
170 175 180	
ctg ggt gtg gta aaa gca aat ggg ctg cta att ttg cag acc cgg aaa	624
Leu Gly Val Val Lys Ala Asn Gly Leu Leu Ile Leu Gln Thr Arg Lys	
185 190 195	
cca cat act gga aac cac cta gaa aca agt ggt ggg atg gtt acc atg	672
Pro His Thr Gly Asn His Leu Glu Thr Ser Gly Gly Met Val Thr Met	
200 205 210 215	

gtg aag aag tgg ttg tta ttg atg act ttt atg gct ggc tgc cct ggg Val Lys Lys Trp Leu Leu Leu Met Thr Phe Met Ala Gly Cys Pro Gly 220 225 230	720
atg atc tac tga gac tgt gtg atc gat atc cat tga ctg tag aga cta Met Ile Tyr Asp Cys Val Ile Asp Ile His Leu Arg Leu 235 240	768
aag gtg gaa ctg tac ctt ttt tgg ccc gca gta ttc tga tta cca gca Lys Val Glu Leu Tyr Leu Phe Trp Pro Ala Val Phe Leu Pro Ala 245 250 255	816
atc aga ccc cgt tgg aat ggt act cct caa ctg ctg tcc cag ctg tag Ile Arg Pro Arg Trp Asn Gly Thr Pro Gln Leu Leu Ser Gln Leu 260 265 270	864
aag ctc ttt atc gga gga tta ctt cct tgg tat ttt gga aga atg cta Lys Leu Phe Ile Gly Gly Leu Leu Pro Trp Tyr Phe Gly Arg Met Leu 275 280 285 290	912
cag aac aat cca cgg agg aag ggg gcc agt tgc tca ccc ttt ccc ccc Gln Asn Asn Pro Arg Arg Lys Gly Ala Ser Ser Ser Pro Phe Pro Pro 295 300 305	960
cat gcc ctg aat ttc cat atg aaa taa att act gag tct ttt tta tca His Ala Leu Asn Phe His Met Lys Ile Thr Glu Ser Phe Leu Ser 310 315 320	1008
ctt cgt aat ggt ttt tat tat tca tta agg gtt aag tgg ggg gtc ttt Leu Arg Asn Gly Phe Tyr Tyr Ser Leu Arg Val Lys Trp Gly Val Phe 325 330 335	1056
aaa att aaa ttc tct gaa ttg tac ata cat ggt tac acg gat att gta Lys Ile Lys Phe Ser Glu Leu Tyr Ile His Gly Tyr Thr Asp Ile Val 340 345 350	1104
ttc ctg gtc gta tat act gtt ttc gaa cgc agt gcc gag gcc tac gtg Phe Leu Val Val Tyr Thr Phe Glu Arg Ser Ala Glu Ala Tyr Val 355 360 365	1152
gtc tac att tcc agc agt ttg tag tct cag cca cag ctg gtt tct ttt Val Tyr Ile Ser Ser Ser Leu Ser Gln Pro Gln Leu Val Ser Phe 370 375 380	1200
gtt gtt tgg ttg gaa gta atc aat agt gaa atc tag gac agg ttt ggg Val Val Trp Leu Glu Val Ile Asn Ser Glu Ile Asp Arg Phe Gly 385 390 395	1248
ggt aaa gta ccg gga gtg gta gga gaa ggg ctg ggt tat ggt atg gcg Gly Lys Val Pro Gly Val Val Gly Glu Gly Leu Gly Tyr Gly Met Ala 400 405 410 415	1296
gga gga gta gtt tac ata ggg gtc ata ggt gag ggc tgt ggc ctt tgt Gly Gly Val Val Tyr Ile Gly Val Ile Gly Glu Gly Cys Gly Leu Cys 420 425 430	1344

tac	aaa	gtt	atc	atc	taa	aat	aac	agc	act	gga	gcc	cac	tcc	cct	gtc	1392
Tyr	Lys	Val	Ile	Ile		Asn	Asn	Ser	Thr	Gly	Ala	His	Ser	Pro	Val	
			435						440						445	

acc	ctg	ggt	gat	cgg	gga	gca	ggg	cca	gaa	ttc	aac	ctt	aac	ctt	tct	1440
Thr	Leu	Gly	Asp	Arg	Gly	Ala	Gly	Pro	Glu	Phe	Asn	Leu	Asn	Leu	Ser	
			450					455					460			

tat	tct	gta	gta	ttc	aaa	ggg	cac	aga	gcg	ggg	gtt	tga	ccc	ccc	tcc	1488
Tyr	Ser	Val	Val	Phe	Lys	Gly	His	Arg	Ala	Gly	Val		Pro	Pro	Ser	
		465					470						475			

tgg	ggg	aag	aaa	gtc	att	aat	att	gaa	tct	cat	cat	gtc	cac	cgc	cca	1536
Trp	Gly	Lys	Lys	Val	Ile	Asn	Ile	Glu	Ser	His	His	Val	His	Arg	Pro	
		480					485					490				

gga	ggg	cgt	tct	gac	tgt	ggt	tcg	ctt	gac	agt	ata	tcc	gaa	ggt	gcg	1584
Gly	Gly	Arg	Ser	Asp	Cys	Gly	Ser	Leu	Asp	Ser	Ile	Ser	Glu	Gly	Ala	
		495				500					505					

gga	gag	gcg	ggt	gtt	gaa	gat	gcc	att	ttt	cct	tct	cca	gcg	gta	acg	1632
Gly	Glu	Ala	Gly	Val	Glu	Asp	Ala	Ile	Phe	Pro	Ser	Pro	Ala	Val	Thr	
510					515					520					525	

gtg	gcg	ggg	gtg	gac	gag	cca	ggg	gcg	gcg	gcg	gag	gat	ctg	gcc	aag	1680
Val	Ala	Gly	Val	Asp	Glu	Pro	Gly	Ala	Ala	Ala	Glu	Asp	Leu	Ala	Lys	
				530					535					540		

atg	gct	gcg	ggg	gcg	gtg	tct	tct	tct	tcg	gta	acg	cct	cct	tgg	ata	1728
Met	Ala	Ala	Gly	Ala	Val	Ser	Ser	Ser	Ser	Val	Thr	Pro	Pro	Trp	Ile	
			545					550					555			

cgt	cat	atc	tga	aaa	cga	aag	aag	tgc	gct	gta	agt	att				1767
Arg	His	Ile		Lys	Arg	Lys	Lys	Cys	Ala	Val	Ser	Ile				
		560						565								

<210> 16

<211> 569

<212> PRT

<213> Type B PWD circovirus

<400> 16

Thr	Ser	Ala	Leu	Arg	Gln	Arg	Gln	His	Leu	Gly	Ser	Thr	Ser	Ala	Ala
1				5					10					15	

Thr Cys Pro Ala Arg Arg Met Glu Glu Ala Asp Pro Asn Pro Ile Lys  
 20 25 30

Gly Gly Cys Ser Leu Ile Ile Leu Pro Lys Thr Ser Ala Arg Lys Tyr  
 35 40 45

Gly Ile Phe Gln Tyr Pro Tyr Leu Ile Ile Leu Leu Leu Ala Arg Arg  
 50 55 60

Val Met Arg Lys Asp Glu His Leu Thr Ser Arg Gly Ser Leu Ile Leu  
 65 70 75 80

Arg Ser Arg Leu Leu Ile Lys Ser Gly Ile Trp Val Pro Ala Ala Thr  
 85 90 95

Ser Arg Lys Arg Lys Glu Gln Ile Ser Arg Ile Lys Asn Thr Ala Val  
 100 105 110

Lys Lys Ala Thr Tyr Trp Ser Val Glu Leu Leu Asp Leu Arg Asp Asn  
 115 120 125

Gly Val Thr Cys Leu Leu Leu Val Pro Cys Trp Arg Ala Gly Val Trp  
 130 135 140

Pro Leu Gln Ser Ser Thr Leu Arg Leu Ser Glu Ile Ser Ala Gly Trp  
 145 150 155 160

Leu Asn Phe Lys Ala Gly Lys Cys Arg Ser Val Ile Gly Arg Leu Met  
 165 170 175

Tyr Thr Ser Leu Trp Gly His Leu Gly Val Val Lys Ala Asn Gly Leu  
 180 185 190

Leu Ile Leu Gln Thr Arg Lys Pro His Thr Gly Asn His Leu Glu Thr  
 195 200 205

Ser Gly Gly Met Val Thr Met Val Lys Lys Trp Leu Leu Leu Met Thr  
 210 215 220

Phe Met Ala Gly Cys Pro Gly Met Ile Tyr Asp Cys Val Ile Asp Ile  
 225 230 235 240

122

His Leu Arg Leu Lys Val Glu Leu Tyr Leu Phe Trp Pro Ala Val Phe  
245 250 255

Leu Pro Ala Ile Arg Pro Arg Trp Asn Gly Thr Pro Gln Leu Leu Ser  
260 265 270

Gln Leu Lys Leu Phe Ile Gly Gly Leu Leu Pro Trp Tyr Phe Gly Arg  
275 280 285

Met. Leu Gln Asn Asn Pro Arg Arg Lys Gly Ala Ser Ser Ser Pro Phe  
290 295 300

Pro Pro His Ala Leu Asn Phe His Met Lys Ile Thr Glu Ser Phe Leu  
305 310 315 320

Ser Leu Arg Asn Gly Phe Tyr Tyr Ser Leu Arg Val Lys Trp Gly Val  
325 330 335

Phe Lys Ile Lys Phe Ser Glu Leu Tyr Ile His Gly Tyr Thr Asp Ile  
340 345 350

Val Phe Leu Val Val Tyr Thr Val Phe Glu Arg Ser Ala Glu Ala Tyr  
355 360 365

Val Val Tyr Ile Ser Ser Ser Leu Ser Gln Pro Gln Leu Val Ser Phe  
370 375 380

Val Val Trp Leu Glu Val Ile Asn Ser Glu Ile Asp Arg Phe Gly Gly  
385 390 395 400

Lys Val Pro Gly Val Val Gly Glu Gly Leu Gly Tyr Gly Met Ala Gly  
405 410 415

Gly Val Val Tyr Ile Gly Val Ile Gly Glu Gly Cys Gly Leu Cys Tyr  
420 425 430

Lys Val Ile Ile Asn Asn Ser Thr Gly Ala His Ser Pro Val Thr Leu  
435 440 445

Gly Asp Arg Gly Ala Gly Pro Glu Phe Asn Leu Asn Leu Ser Tyr Ser  
450 455 460

Val Val Phe Lys Gly His Arg Ala Gly Val Pro Pro Ser Trp Gly Lys  
465 470 475 480

Lys Val Ile Asn Ile Glu Ser His His Val His Arg Pro Gly Gly Arg  
485 490 495

Ser Asp Cys Gly Ser Leu Asp Ser Ile Ser Glu Gly Ala Gly Glu Ala  
500 505 510

Gly Val Glu Asp Ala Ile Phe Pro Ser Pro Ala Val Thr Val Ala Gly  
515 520 525

Val Asp Glu Pro Gly Ala Ala Ala Glu Asp Leu Ala Lys Met Ala Ala  
530 535 540

Gly Ala Val Ser Ser Ser Ser Val Thr Pro Pro Trp Ile Arg His Ile  
545 550 555 560

Lys Arg Lys Lys Cys Ala Val Ser Ile  
565

<210> 17

<211> 542

<212> PRT

<213> Type B PWD circovirus

<400> 17

Pro Ala His Phe Gly Ser Gly Ser Thr Ser Ala Ala Pro Gln Gln Gln  
1 5 10 15

His Ala Gln Gln Glu Glu Trp Lys Lys Arg Thr Pro Thr Pro Lys Val  
20 25 30

Gly Val His Ser Glu Ser Phe Arg Arg Arg Ala Gln Glu Asn Thr Gly  
35 40 45

Ser Ser Asn Ile Pro Ile Leu Phe Tyr Cys Trp Arg Gly Gly Gly Arg  
50 55 60

Thr	Asn	Thr	Ser	Pro	Pro	Gly	Val	Arg	Phe	Cys	Glu	Glu	Ala	Asp	Phe	
65					70					75					80	
Ser	Glu	Val	Val	Phe	Gly	Cys	Pro	Leu	Pro	His	Arg	Glu	Ser	Glu	Arg	
				85					90					95		
Asn	Arg	Ser	Ala	Glu	Arg	Ile	Leu	Gln	Arg	Arg	Gln	Leu	Thr	Asp	Gly	
			100					105					110			
Val	Trp	Ser	Ser	Ile	Ser	Gly	Thr	Thr	Glu	Pro	Val	Tyr	Cys	Cys	Glu	
		115					120					125				
Tyr	Leu	Val	Gly	Glu	Arg	Glu	Ser	Gly	Asp	Arg	Cys	Arg	Ala	Ala	Pro	
	130					135					140					
Cys	Asn	Val	Cys	Gln	Lys	Phe	Pro	Arg	Ala	Gly	Thr	Phe	Glu	Ser	Glu	
145					150					155					160	
Arg	Glu	Asn	Ala	Glu	Ala	Cys	Thr	Arg	His	Cys	Gly	Ala	Thr	Trp	Val	
				165					170					175		
Trp	Lys	Gln	Met	Gly	Cys	Phe	Cys	Arg	Pro	Gly	Asn	His	Ile	Leu	Glu	
			180					185					190			
Thr	Thr	Lys	Gln	Val	Val	Gly	Trp	Leu	Pro	Trp	Arg	Ser	Gly	Cys	Tyr	
		195					200					205				
Leu	Leu	Trp	Leu	Ala	Ala	Leu	Gly	Ser	Thr	Glu	Thr	Val	Ser	Ile	Ser	
	210					215						220				
Ile	Asp	Cys	Arg	Asp	Arg	Trp	Asn	Cys	Thr	Phe	Phe	Gly	Pro	Gln	Tyr	
225					230					235					240	
Ser	Asp	Tyr	Gln	Gln	Ser	Asp	Pro	Val	Gly	Met	Val	Leu	Leu	Asn	Cys	
			245						250					255		
Cys	Pro	Ser	Cys	Arg	Ser	Ser	Leu	Ser	Glu	Asp	Tyr	Phe	Leu	Gly	Ile	
			260					265					270			
Leu	Glu	Glu	Cys	Tyr	Arg	Thr	Ile	His	Gly	Gly	Arg	Gly	Pro	Val	Arg	
		275					280					285				
His	Pro	Phe	Pro	Pro	Met	Pro	Asn	Lys	Leu	Leu	Ser	Leu	Phe	Tyr	His	
						295					300					
Phe	Val	Met	Val	Phe	Ile	Ile	His	Gly	Leu	Ser	Gly	Gly	Ser	Leu	Lys	
305					310					315					320	
Leu	Asn	Ser	Leu	Asn	Cys	Thr	Tyr	Met	Val	Thr	Arg	Ile	Leu	Tyr	Ser	
				325					330					335		
Trp	Ser	Tyr	Ile	Leu	Phe	Ser	Asn	Ala	Val	Pro	Arg	Pro	Thr	Trp	Ser	
			340					345					350			



Thr Phe Pro Ala Val Cys Ser Leu Ser His Ser Trp Phe Leu Leu Leu  
355 360 365

Phe Gly Trp Lys Ser Ile Val Lys Ser Arg Thr Gly Leu Gly Val Lys  
370 375 380

Tyr Arg Glu Trp Glu Lys Gly Trp Val Met Val Trp Arg Glu Glu Val  
385 390 395 400

Arg Ala Val Ala Phe Val Thr Lys Leu Ser Ser Lys Ile Thr Ala Leu  
405 410 415

Glu Pro Thr Pro Leu Ser Pro Trp Val Ile Gly Glu Gln Gly Gln Asn  
420 425 430

Ser Thr Leu Thr Phe Leu Ile Leu Tyr Ser Lys Gly Thr Glu Arg Gly  
435 440 445

Phe Asp Pro Pro Pro Gly Gly Arg Lys Ser Leu Ile Leu Asn Leu Ile  
450 455 460

Met Ser Thr Ala Gln Glu Gly Val Leu Thr Val Val Arg Leu Thr Val  
465 470 475 480

Tyr Pro Lys Val Arg Glu Arg Arg Val Leu Lys Met Pro Phe Phe Leu  
485 490 495

Leu Gln Arg Arg Trp Arg Gly Trp Thr Ser Gln Gly Arg Arg Arg Arg  
500 505 510

Ile Trp Pro Arg Trp Leu Arg Gly Arg Cys Leu Leu Leu Arg Arg Leu  
515 520 525

Leu Gly Tyr Val Ile Ser Glu Asn Glu Arg Ser Ala Leu Val  
530 535 540

<210> 18

<211> 566

<212> PRT

<213> Type B PWD circovirus

<400> 18

Gln Arg Thr Ser Ala Ala Ala Ala Pro Arg Gln His Leu Ser Ser Asn  
1 5 10 15

Met Pro Ser Lys Lys Asn Gly Arg Ser Gly Pro Gln Pro His Lys Arg  
20 25 30

Trp	Val	Phe	Thr	Leu	Asn	Asn	Pro	Ser	Glu	Asp	Glu	Arg	Lys	Lys	Ile	35	40	45
Arg	Asp	Leu	Pro	Ile	Ser	Leu	Phe	Asp	Tyr	Phe	Ile	Val	Gly	Glu	Glu	50	55	60
Gly	Asn	Glu	Glu	Gly	Arg	Thr	Pro	His	Leu	Gln	Gly	Phe	Ala	Asn	Phe	65	70	75
Val	Lys	Lys	Gln	Thr	Phe	Asn	Lys	Val	Lys	Trp	Tyr	Leu	Gly	Ala	Arg	85	90	95
Cys	His	Ile	Glu	Lys	Ala	Lys	Gly	Thr	Asp	Gln	Gln	Asn	Lys	Glu	Tyr	100	105	110
Cys	Ser	Lys	Glu	Gly	Asn	Leu	Leu	Met	Glu	Cys	Gly	Ala	Pro	Arg	Ser	115	120	125
Gln	Gly	Gln	Arg	Ser	Asp	Leu	Ser	Thr	Ala	Val	Ser	Thr	Leu	Leu	Glu	130	135	140
Ser	Gly	Ser	Leu	Val	Thr	Val	Ala	Glu	Gln	His	Pro	Val	Thr	Phe	Val	145	150	155
Arg	Asn	Phe	Arg	Gly	Leu	Ala	Glu	Leu	Leu	Lys	Val	Ser	Gly	Lys	Met	165	170	175
Gln	Lys	Arg	Asp	Trp	Lys	Thr	Asn	Val	His	Val	Ile	Val	Gly	Pro	Pro	180	185	190
Gly	Cys	Gly	Lys	Ser	Lys	Trp	Ala	Ala	Asn	Phe	Ala	Asp	Pro	Glu	Thr	195	200	205
Thr	Tyr	Trp	Lys	Pro	Pro	Arg	Asn	Lys	Trp	Trp	Asp	Gly	Tyr	His	Gly	210	215	220
Glu	Glu	Val	Val	Val	Ile	Asp	Asp	Phe	Tyr	Gly	Trp	Leu	Pro	Trp	Asp	225	230	235
Asp	Leu	Leu	Arg	Leu	Cys	Asp	Arg	Tyr	Pro	Leu	Thr	Val	Glu	Thr	Lys	245	250	255
Gly	Gly	Thr	Val	Pro	Phe	Leu	Ala	Arg	Ser	Ile	Leu	Ile	Thr	Ser	Asn	260	265	270
Gln	Thr	Pro	Leu	Glu	Trp	Tyr	Ser	Ser	Thr	Ala	Val	Pro	Ala	Val	Glu	275	280	285
Ala	Leu	Tyr	Arg	Arg	Ile	Thr	Ser	Leu	Val	Phe	Trp	Lys	Asn	Ala	Thr	290	295	300
Glu	Gln	Ser	Thr	Glu	Glu	Gly	Gly	Gln	Phe	Val	Thr	Leu	Ser	Pro	Pro	305	310	315
																		320

Cys Pro Glu Phe Pro Tyr Glu Ile Asn Tyr Val Phe Phe Ile Thr Ser  
 325 330 335  
 Trp Phe Leu Leu Phe Ile Lys Gly Val Gly Gly Leu Ile Val His Thr  
 340 345 350  
 Trp Leu His Gly Tyr Cys Ile Pro Gly Arg Ile Tyr Cys Phe Arg Thr  
 355 360 365  
 Gln Cys Arg Gly Leu Arg Gly Leu His Phe Gln Gln Phe Val Val Ser  
 370 375 380  
 Ala Thr Ala Gly Phe Phe Cys Cys Leu Val Gly Ser Asn Gln Asn Leu  
 385 390 395 400  
 Gly Gln Val Trp Gly Ser Thr Gly Ser Gly Arg Arg Arg Ala Gly Leu  
 405 410 415  
 Trp Tyr Gly Gly Arg Ser Ser Leu His Arg Gly His Arg Gly Leu Trp  
 420 425 430  
 Pro Leu Leu Gln Ser Tyr His Leu Lys Gln His Trp Ser Pro Leu Pro  
 435 440 445  
 Cys His Pro Gly Ser Gly Ser Arg Ala Arg Ile Gln Pro Pro Phe Leu  
 450 455 460  
 Phe Cys Ser Ile Gln Arg Ala Gln Ser Gly Gly Leu Thr Pro Leu Leu  
 465 470 475 480  
 Gly Glu Glu Ser His Ile Ser Ser Cys Pro Pro Pro Arg Arg Ala Phe  
 485 490 495  
 Leu Trp Phe Ala Gln Tyr Ile Arg Arg Cys Gly Arg Gly Gly Cys Arg  
 500 505 510  
 Cys His Phe Ser Phe Ser Ser Gly Asn Gly Gly Gly Gly Gly Arg Ala  
 515 520 525  
 Arg Gly Gly Gly Gly Gly Ser Gly Gln Asp Gly Cys Gly Gly Gly Val  
 530 535 540  
 Phe Phe Phe Gly Asn Ala Ser Leu Asp Thr Ser Tyr Leu Lys Thr Lys  
 545 550 555 560  
 Glu Val Arg Cys Lys Tyr  
 565

<210> 19

<211> 1767

<212> DNA

<213> Type B PWD circovirus

<400> 19

aatacttaca ggcacttct ttcgttttca gatatgacgt atccaaggag gcgttaccga	60
agaagaagac accgcccccg cagccatctt ggccagatcc tccgccgccg cccctggctc	120
gtccaccccc gccaccgtta ccgctggaga aggaaaaatg gcattcttcaa caccgcctc	180
tcccgcacct tcggatatac tgtcaagcga accacagtca gaacgcctc ctggggcgtg	240
gacatgatga gattcaatat taatgacttt cttccccag gaggggggtc aaacccccgc	300
tctgtgccct ttgaatacta cagaataaga aagggttaagg ttgaattctg gccctgctcc	360
ccgatcacc cagggtgacag gggagtgggc tccagtgtg ttattttaga tgataacttt	420
gtaacaaagg ccacagccct cacctatgac ccctatgtaa actactctc ccgccatacc	480
ataaccagc ccttctccta ccactcccg tactttacc ccaaactgt cctagatttc	540
actattgatt acttccaacc aaacaacaaa agaaaccagc tgtggctgag actacaaact	600
gctggaaatg tagaccagc aggcctcggc actgcgttcg aaaacagtat atacgaccag	660
gaatacaata tccgtgtaac catgtatgta caattcagag aatttaattt taaagacccc	720
ccacttaacc cttaatgaat aataaaaacc attacgaagt gataaaaaag actcagtaat	780
ttatttcata tggaaattca gggcatgggg gggaaagggt gacgaactgg ccccttctc	840
ccgtggattg ttctgtagca ttcttccaaa ataccaagga agtaatctc cgataaagag	900
cttctacagc tgggacagca gttgaggagt accattccaa cgggggtctga ttgctggtaa	960
tcagaatact gcgggccaaa aaaggtagag ttccacctt agtctctaca gtcaatggat	1020
atcgatcaca cagtctcagt agatcatccc agggcagcca gccataaaag tcatcaataa	1080
caaccacttc ttcacatgg taaccatccc accacttggt tctaggtggt ttccagtatg	1140
tggtttccgg gtctgcaaaa ttagcagccc atttgctttt accacacca ggtggcccca	1200
caatgacgtg tacattagtc ttccaatcac gcttctgcat tttccgctc actttcaaaa	1260
gttcagccag ccgcgggaaa tttctgacaa acgttacagg gtgctgctc gcaacggtca	1320
ccagactccc gctctccaac aaggtagtca cagcagtaga caggctactc cgttgctcct	1380
gagatctagg agctccacac tccatcagta agttgccttc ttactgcag tattctttat	1440
tctgctgac tggttccttc gctttctcga tgtggcagcg ggcacccaaa taccattca	1500
ctttattaaa agtctgcttc ttcacaaaat tagcgaaccc ctggaggtga ggtgttcgtc	1560

cttcctcatt accctcctcg ccaacaataa aataatcaaa tagggatatt ggaagatccc 1620  
gtatttttctt gcgctcgtct tcggaaggat tattcagagt gaacaccac cttttatggg 1680  
gttgggggtcc gctttcttcca ttcttcttgc tgggcatgtt gctgctgagg tgctgccgag 1740  
gtgctgccgc tgccgaagtg cgctggt 1767

<210> 20

<211> 567

<212> PRT

<213> Type B PWD circovirus

<400> 20

Gly	Ala	Cys	Lys	Pro	Leu	Pro	Leu	Val	Glu	Ala	Ala	Gly	Cys	Cys	Cys	1	5	10	15
Ala	Trp	Cys	Ser	Ser	His	Phe	Phe	Arg	Val	Gly	Val	Gly	Tyr	Phe	Thr	20	25	30	
Pro	Thr	Glu	Ser	Tyr	Asp	Lys	Arg	Leu	Arg	Ala	Cys	Ser	Phe	Val	Pro	35	40	45	
Asp	Glu	Leu	Ile	Gly	Ile	Gln	Asn	Asn	Gln	Gln	Arg	Pro	Pro	Tyr	His	50	55	60	
Pro	Leu	Val	Phe	Val	Glu	Gly	Gly	Pro	Thr	Arg	Asn	Gln	Ser	Ser	Ala	65	70	75	80
Ser	Lys	Tyr	Leu	Ser	Thr	Thr	Asn	Pro	His	Gly	Ser	Gly	Cys	Arg	Ser	85	90	95	
Leu	Ser	Leu	Phe	Leu	Asp	Ala	Ser	Tyr	Leu	Ile	Ser	Cys	Tyr	Leu	Leu	100	105	110	
Cys	Ser	Val	Ser	Pro	Thr	His	Leu	Glu	Ile	Glu	Pro	Val	Val	Ser	His	115	120	125	
Gly	Thr	Gln	Gln	Ser	Tyr	Arg	Thr	Pro	Ser	Arg	Ser	Asp	Pro	Ser	Arg	130	135	140	
Gln	Leu	Ala	Ala	Gly	Gln	Leu	Thr	Gln	Phe	Asn	Gly	Arg	Ala	Pro	Gln	145	150	155	160
Val	Lys	Ser	Leu	Ser	Arg	Ser	Phe	Ala	Ser	Ala	His	Asn	Ser	Ser	His	165	170	175	

Val	Arg	Gln	Pro	Ala	Val	Gln	Thr	His	Tyr	Phe	Cys	Ile	Pro	Gln	Asn	180	185	190
Gln	Leu	Gly	Pro	Phe	Trp	Met	Ser	Ser	Val	Val	Phe	Cys	Thr	Thr	Pro	195	200	205
His	Asn	Gly	His	His	Leu	Leu	Pro	Gln	Gln	His	Ser	Lys	His	Ser	Ala	210	215	220
Ala	Arg	Pro	His	Asp	Val	Ser	Val	Thr	His	Asp	Ile	Asp	Met	Ser	Gln	225	230	235
Leu	Ser	Leu	His	Phe	Gln	Val	Lys	Lys	Pro	Gly	Cys	Tyr	Glu	Ser	Trp	245	250	255
Cys	Asp	Ser	Gly	Thr	Pro	Ile	Thr	Ser	Arg	Leu	Gln	Gln	Gly	Leu	Gln	260	265	270
Leu	Leu	Glu	Lys	Asp	Ser	Ser	Lys	Arg	Pro	Ile	Lys	Ser	Ser	His	Leu	275	280	285
Val	Ile	Trp	Pro	Pro	Leu	Pro	Gly	Thr	Arg	Gly	Lys	Gly	Gly	Met	Gly	290	295	300
Gln	Ile	Glu	Met	His	Phe	Leu	Asn	Ser	Leu	Arg	Lys	Lys	Thr	Ile	Thr	305	310	315
Lys	Ile	Ile	Pro	Asn	Leu	Pro	Pro	Asp	Lys	Phe	Asn	Phe	Glu	Arg	Phe	325	330	335
Gln	Val	Tyr	Met	Thr	Val	Arg	Ile	Asn	Tyr	Glu	Gln	Asp	Tyr	Ile	Ser	340	345	350
Asn	Glu	Phe	Ala	Thr	Gly	Leu	Gly	Val	His	Asp	Val	Asn	Gly	Ala	Thr	355	360	365
Gln	Leu	Arg	Leu	Trp	Leu	Gln	Asn	Arg	Lys	Asn	Asn	Pro	Gln	Phe	Tyr	370	375	380
Asp	Ile	Thr	Phe	Asp	Leu	Val	Pro	Lys	Pro	Thr	Phe	Tyr	Arg	Ser	His	385	390	395
Tyr	Ser	Phe	Pro	Gln	Thr	Ile	Thr	His	Arg	Ser	Ser	Tyr	Asn	Val	Tyr	405	410	415
Pro	Asp	Tyr	Thr	Leu	Ala	Thr	Ala	Lys	Thr	Val	Pro	Asn	Asp	Asp	Leu	420	425	430
Ile	Val	Ala	Ser	Ser	Gly	Val	Gly	Arg	Asp	Gly	Gln	Thr	Ile	Pro	Ser	435	440	445
Cys	Pro	Trp	Phe	Glu	Val	Lys	Val	Lys	Arg	Ile	Arg	Tyr	Tyr	Glu	Phe	450	455	460

Pro Val Ser Arg Pro Asn Ser Gly Gly Gly Pro Pro Leu Phe Asp Asn  
465 470 475 480

Ile Asn Phe Arg Met Met Asp Val Ala Trp Ser Pro Thr Arg Val Thr  
485 490 495

Thr Arg Lys Val Thr Tyr Gly Phe Thr Arg Ser Leu Arg Thr Asn Phe  
500 505 510

Ile Gly Asn Lys Arg Arg Trp Arg Tyr Arg His Arg Pro His Val Leu  
515 520 525

Trp Pro Arg Arg Arg Leu Ile Gln Gly Leu His Ser Arg Pro Arg His  
530 535 540

Arg Arg Arg Arg Tyr Arg Arg Arg Pro Tyr Thr Met Asp Ser Phe Ser  
545 550 555 560

Leu Leu Ala Ser Tyr Thr Asn  
565

<210> 21

<211> 566

<212> PRT

<213> Type B PWD circovirus

<400> 21

Trp Arg Val Glu Ala Ala Ala Ala Gly Arg Cys Cys Arg Leu Leu Leu  
1 5 10 15

Met Gly Leu Leu Phe Phe Pro Leu Leu Pro Gly Trp Gly Trp Leu Leu  
20 25 30

His Thr Asn Val Arg Phe Leu Gly Glu Ser Ser Ser Arg Leu Phe Ile  
35 40 45

Arg Ser Arg Gly Ile Asp Arg Asn Ser Lys Ile Thr Pro Ser Ser Pro  
50 55 60

Leu Ser Ser Pro Arg Val Gly Arg Trp Pro Asn Ala Leu Lys Thr Phe  
65 70 75 80

Phe Cys Val Lys Leu Leu Thr Phe His Tyr Lys Pro Ala Arg Gln Trp  
85 90 95

Met Ser Phe Ala Phe Pro Val Ser Cys Phe Leu Ser Tyr Gln Leu Leu  
100 105 110

132

Ser Pro Leu Lys Ser Ile Ser His Pro Ala Gly Leu Asp Pro Cys Arg  
 115 120 125  
 Leu Ser Arg Asp Val Ala Thr Leu Val Lys Asn Ser Leu Pro Leu Arg  
 130 135 140  
 Thr Val Thr Ala Ser Cys Cys Gly Thr Val Asn Thr Leu Phe Lys Arg  
 145 150 155 160  
 Pro Ser Ala Ser Ser Lys Phe Thr Leu Pro Phe Ile Cys Phe Arg Ser  
 165 170 175  
 Gln Phe Val Leu Thr Cys Thr Met Thr Pro Gly Gly Pro His Pro Leu  
 180 185 190  
 Leu Leu His Ala Ala Leu Lys Ala Ser Gly Ser Val Val Tyr Gln Phe  
 195 200 205  
 Gly Gly Leu Phe Leu His His Ser Pro Trp Pro Ser Ser Thr Thr Thr  
 210 215 220  
 Ile Ser Ser Lys Pro Gln Ser Gly Gln Ser Ser Arg Ser Leu Ser His  
 225 230 235 240  
 Ser Arg Tyr Gly Asn Val Thr Ser Val Leu Pro Pro Val Thr Gly Lys  
 245 250 255  
 Lys Ala Arg Leu Ile Arg Ile Val Leu Leu Val Gly Asn Ser His Tyr  
 260 265 270  
 Glu Glu Val Ala Thr Gly Ala Thr Ser Ala Arg Arg Leu Ile Val Glu  
 275 280 285  
 Lys Thr Asn Gln Phe Phe Ala Val Ser Cys Asp Val Ser Ser Pro Pro  
 290 295 300  
 Trp Asn Thr Val Arg Glu Gly Gly His Gly Ser Asn Gly Tyr Ser Ile  
 305 310 315 320  
 Phe Gln Thr Lys Lys Ile Val Glu Tyr His Asn Lys Asn Asn Met Leu  
 325 330 335  
 Pro Thr Pro Pro Arg Phe Ile Arg Gln Ile Thr Cys Val His Asn Cys  
 340 345 350  
 Pro Tyr Gln Ile Gly Pro Arg Ile Tyr Gln Lys Arg Val Cys His Arg  
 355 360 365  
 Pro Arg Arg Pro Arg Cys Lys Trp Cys Asn Thr Thr Glu Ala Val Ala  
 370 375 380  
 Pro Lys Lys Gln Gln Lys Thr Pro Leu Leu Tyr His Phe Arg Pro Cys  
 385 390 395 400



Thr Gln Pro Tyr Leu Val Pro Leu Pro Leu Leu Leu Ala Pro Asn His  
405 410 415

Tyr Pro Pro Leu Leu Leu Lys Cys Leu Pro Leu His Pro Ser His Gly  
420 425 430

Lys Asn Cys Leu Arg Phe Tyr Cys Cys Gln Leu Gly Ser Gly Gln Gly  
435 440 445

Pro His Asp Pro Leu Leu Ala Leu Ile Gly Gly Lys Lys Asn Gln Leu  
450 455 460

Ile Leu Ala Cys Leu Pro Pro Lys Val Gly Arg Arg Pro Ser Ser Leu  
465 470 475 480

Tyr Gln Ile Glu Asp His Gly Gly Gly Leu Leu Ala Asn Gln Ser His  
485 490 495

Asn Ala Gln Cys Tyr Ile Arg Leu His Pro Leu Pro Pro His Gln Leu  
500 505 510

His Trp Lys Glu Lys Glu Leu Pro Leu Pro Pro Pro Pro Arg Ala  
515 520 525

Leu Pro Pro Pro Pro Pro Asp Pro Trp Ser Pro Gln Pro Pro Pro Thr  
530 535 540

Lys Lys Lys Pro Leu Ala Glu Lys Ser Val Asp Tyr Arg Phe Val Phe  
545 550 555 560

Ser Thr Arg Gln Leu Tyr  
565

<210> 22

<211> 569

<212> PRT

<213> Type B PWD circovirus

<400> 22

Leu Ala Ser Arg Cys Arg Cys Cys Arg Pro Leu Val Glu Ala Ala Val  
1 5 10 15

His Gly Ala Leu Leu Ile Ser Ser Ala Ser Gly Leu Gly Met Phe Pro  
20 25 30

Pro His Glu Ser Gln Ile Ile Arg Gly Phe Val Leu Ala Leu Phe Tyr  
35 40 45

Pro Ile Lys Trp Tyr Gly Lys Ile Ile Lys Asn Asn Ala Leu Leu Thr  
 50 55 60  
 Ile Leu Phe Ser Ser Cys Arg Val Glu Leu Pro Glu Ser Ile Lys His  
 65 70 75 80  
 Leu Leu Leu Ser Lys Ile Phe His Leu Pro Ile Gln Thr Gly Ala Ala  
 85 90 95  
 Val Asp Leu Phe Arg Phe Ser Cys Ile Leu Leu Ile Phe Phe Val Ala  
 100 105 110  
 Thr Phe Phe Ala Val Gln His Leu Thr Ser Ser Arg Ser Arg Leu Ser  
 115 120 125  
 Leu Pro Thr Val Gln Arg Ser Ser His Thr Gly Gln Gln Leu Ala Pro  
 130 135 140  
 Thr Gln His Gly Asn Cys Leu Leu Val Arg Tyr Arg Lys Asp Ser Ile  
 145 150 155 160  
 Glu Ala Pro Gln Ser Phe Lys Gln Phe His Ala Pro Phe His Leu Leu  
 165 170 175  
 Thr Ile Pro Leu Ser Ile Tyr Val Asp Asn His Pro Trp Arg Pro Thr  
 180 185 190  
 Thr Phe Ala Phe Pro Ser Ser Ile Lys Cys Val Arg Phe Gly Cys Val  
 195 200 205  
 Pro Phe Trp Arg Ser Val Leu Pro Pro Ile Thr Val Met Thr Phe Phe  
 210 215 220  
 His Asn Asn Asn Ile Val Lys Ile Ala Pro Gln Gly Pro Ile Ile Gln  
 225 230 235 240  
 Ser Gln Thr Ser Ser Ile Trp Gln Ser Tyr Leu Ser Phe Thr Ser Ser  
 245 250 255  
 Tyr Arg Lys Gln Gly Ala Thr Asn Gln Asn Gly Ala Ile Leu Gly Arg  
 260 265 270  
 Gln Phe Pro Val Gly Ser Ser Asp Trp Ser Tyr Phe Ser Lys Ile Pro  
 275 280 285  
 Pro Asn Ser Gly Gln Tyr Lys Pro Leu Ile Ser Cys Phe Leu Gly Arg  
 290 295 300  
 Leu Phe Pro Ala Leu Glu Asp Gly Lys Gly Gly Trp Ala Arg Phe Lys  
 305 310 315 320  
 Trp Ile Phe Trp Ile Val Ser Asp Lys Lys Asp Ser Arg Leu Pro Lys  
 325 330 335

Glu Asn Leu Thr Leu His Pro Thr Lys Leu Ile Leu Asn Glu Ser Asn  
 340 345 350  
 Tyr Met Cys Pro Val Ser Ile Thr Asn Arg Thr Thr Tyr Val Thr Lys  
 355 360 365  
 Ser Arg Leu Ala Ser Ala Thr Thr Met Glu Leu Leu Lys Tyr Asp Gly  
 370 375 380  
 Cys Ser Thr Glu Lys Thr Thr Gln Asn Ser Thr Ile Leu Leu Ser Ile  
 385 390 395 400  
 Ser Leu Asn Pro Pro Leu Thr Gly Pro Thr Thr Pro Ser Pro Ser Pro  
 405 410 415  
 Pro Ile Ala Pro Pro Thr Thr Met Pro Thr Met Pro Ser Pro Gln Pro  
 420 425 430  
 Arg Gln Leu Thr Ile Met Phe Leu Leu Val Pro Ala Trp Glu Gly Thr  
 435 440 445  
 Val Arg Pro Ser Arg Pro Ala Pro Gly Ser Asn Leu Arg Leu Arg Glu  
 450 455 460  
 Glu Thr Thr Asn Leu Pro Cys Leu Ala Pro Thr Gln Gly Gly Glu Gln  
 465 470 475 480  
 Pro Phe Phe Thr Met Leu Ile Ser Asp Thr Trp Arg Gly Pro Pro Arg  
 485 490 495  
 Glu Ser Gln Pro Glu Ser Ser Leu Ile Asp Ser Pro Ala Pro Ser Ala  
 500 505 510  
 Pro Thr Ser Ser Ala Met Lys Gly Glu Gly Ala Thr Val Thr Ala Pro  
 515 520 525  
 Thr Ser Ser Gly Pro Ala Ala Ala Ser Ser Arg Ala Leu Ile Ala Ala  
 530 535 540  
 Pro Ala Thr Asp Glu Glu Glu Thr Val Gly Gly Gln Ile Arg Ile Gln  
 545 550 555 560  
 Phe Arg Phe Phe His Ala Thr Leu Ile  
 565

<210> 23

<211> 945

<212> DNA

<213> Type B PWD circovirus

<220>

<221> CDS

<222> (1)..(942)

<400> 23

atg ccc agc aag aag aat gga aga agc gga ccc caa ccc cat aaa agg	48
Met Pro Ser Lys Lys Asn Gly Arg Ser Gly Pro Gln Pro His Lys Arg	
1 5 10 15	
tgg gtg ttc act ctg aat aat cct tcc gaa gac gag cgc aag aaa ata	96
Trp Val Phe Thr Leu Asn Asn Pro Ser Glu Asp Glu Arg Lys Lys Ile	
20 25 30	
cgg gat ctt cca ata tcc cta ttt gat tat ttt att gtt ggc gag gag	144
Arg Asp Leu Pro Ile Ser Leu Phe Asp Tyr Phe Ile Val Gly Glu Glu	
35 40 45	
ggt aat gag gaa gga cga aca cct cac ctc cag ggg ttc gct aat ttt	192
Gly Asn Glu Glu Gly Arg Thr Pro His Leu Gln Gly Phe Ala Asn Phe	
50 55 60	
gtg aag aag cag act ttt aat aaa gtg aag tgg tat ttg ggt gcc cgc	240
Val Lys Lys Gln Thr Phe Asn Lys Val Lys Trp Tyr Leu Gly Ala Arg	
65 70 75 80	
tgc cac atc gag aaa gcg aaa gga aca gat cag cag aat aaa gaa tac	288
Cys His Ile Glu Lys Ala Lys Gly Thr Asp Gln Gln Asn Lys Glu Tyr	
85 90 95	
tgc agt aaa gaa ggc aac tta ctg atg gag tgt gga gct cct aga tct	336
Cys Ser Lys Glu Gly Asn Leu Leu Met Glu Cys Gly Ala Pro Arg Ser	
100 105 110	
cag gga caa cgg agt gac ctg tct act gct gtg agt acc ttg ttg gag	384
Gln Gly Gln Arg Ser Asp Leu Ser Thr Ala Val Ser Thr Leu Leu Glu	
115 120 125	
agc ggg agt ctg gtg acc gtt gca gag cag cac cct gta acg ttt gtc	432
Ser Gly Ser Leu Val Thr Val Ala Glu Gln His Pro Val Thr Phe Val	
130 135 140	
aga aat ttc cgc ggg ctg gct gaa ctt ttg aaa gtg agc ggg aaa atg	480
Arg Asn Phe Arg Gly Leu Ala Glu Leu Leu Lys Val Ser Gly Lys Met	
145 150 155 160	
cag aag cgt gat tgg aag act aat gta cac gtc att gtg ggg cca cct	528
Gln Lys Arg Asp Trp Lys Thr Asn Val His Val Ile Val Gly Pro Pro	
165 170 175	

ggg tgt ggt aaa agc aaa tgg gct gct aat ttt gca gac ccg gaa acc	576
Gly Cys Gly Lys Ser Lys Trp Ala Ala Asn Phe Ala Asp Pro Glu Thr	
180 185 190	
aca tac tgg aaa cca cct aga aac aag tgg tgg gat ggt tac cat ggt	624
Thr Tyr Trp Lys Pro Pro Arg Asn Lys Trp Trp Asp Gly Tyr His Gly	
195 200 205	
gaa gaa gtg gtt gtt att gat gac ttt tat ggc tgg ctg ccc tgg gat	672
Glu Glu Val Val Val Ile Asp Asp Phe Tyr Gly Trp Leu Pro Trp Asp	
210 215 220	
gat cta ctg aga ctg tgt gat cga tat cca ttg act gta gag act aaa	720
Asp Leu Leu Arg Leu Cys Asp Arg Tyr Pro Leu Thr Val Glu Thr Lys	
225 230 235 240	
ggg gga act gta cct ttt ttg gcc cgc agt att ctg att acc agc aat	768
Gly Gly Thr Val Pro Phe Leu Ala Arg Ser Ile Leu Ile Thr Ser Asn	
245 250 255	
cag acc ccg ttg gaa tgg tac tcc tca act gct gtc cca gct gta gaa	816
Gln Thr Pro Leu Glu Trp Tyr Ser Ser Thr Ala Val Pro Ala Val Glu	
260 265 270	
gct ctt tat cgg agg att act tcc ttg gta ttt tgg aag aat gct aca	864
Ala Leu Tyr Arg Arg Ile Thr Ser Leu Val Phe Trp Lys Asn Ala Thr	
275 280 285	
gaa caa tcc acg gag gaa ggg ggc cag ttc gtc acc ctt tcc ccc cca	912
Glu Gln Ser Thr Glu Glu Gly Gly Gln Phe Val Thr Leu Ser Pro Pro	
290 295 300	
tgc cct gaa ttt cca tat gaa ata aat tac tga	945
Cys Pro Glu Phe Pro Tyr Glu Ile Asn Tyr	
305 310	

<210> 24

<211> 314

<212> PRT

<213> Type B PWD circovirus

<400> 24

Met Pro Ser Lys Lys Asn Gly Arg Ser Gly Pro Gln Pro His Lys Arg
1 5 10 15

Trp Val Phe Thr Leu Asn Asn Pro Ser Glu Asp Glu Arg Lys Lys Ile
20 25 30

Arg Asp Leu Pro Ile Ser Leu Phe Asp Tyr Phe Ile Val Gly Glu Glu  
35 40 45

Gly Asn Glu Glu Gly Arg Thr Pro His Leu Gln Gly Phe Ala Asn Phe  
50 55 60

Val Lys Lys Gln Thr Phe Asn Lys Val Lys Trp Tyr Leu Gly Ala Arg  
65 70 75 80

Cys His Ile Glu Lys Ala Lys Gly Thr Asp Gln Gln Asn Lys Glu Tyr  
85 90 95

Cys Ser Lys Glu Gly Asn Leu Leu Met Glu Cys Gly Ala Pro Arg Ser  
100 105 110

Gln Gly Gln Arg Ser Asp Leu Ser Thr Ala Val Ser Thr Leu Leu Glu  
115 120 125

Ser Gly Ser Leu Val Thr Val Ala Glu Gln His Pro Val Thr Phe Val  
130 135 140

Arg Asn Phe Arg Gly Leu Ala Glu Leu Leu Lys Val Ser Gly Lys Met  
145 150 155 160

Gln Lys Arg Asp Trp Lys Thr Asn Val His Val Ile Val Gly Pro Pro  
165 170 175

Gly Cys Gly Lys Ser Lys Trp Ala Ala Asn Phe Ala Asp Pro Glu Thr  
180 185 190

Thr Tyr Trp Lys Pro Pro Arg Asn Lys Trp Trp Asp Gly Tyr His Gly  
195 200 205

Glu Glu Val Val Val Ile Asp Asp Phe Tyr Gly Trp Leu Pro Trp Asp  
210 215 220

Asp Leu Leu Arg Leu Cys Asp Arg Tyr Pro Leu Thr Val Glu Thr Lys  
225 230 235 240

Gly Gly Thr Val Pro Phe Leu Ala Arg Ser Ile Leu Ile Thr Ser Asn  
245 250 255

Gln Thr Pro Leu Glu Trp Tyr Ser Ser Thr Ala Val Pro Ala Val Glu  
 260 265 270

Ala Leu Tyr Arg Arg Ile Thr Ser Leu Val Phe Trp Lys Asn Ala Thr  
 275 280 285

Glu Gln Ser Thr Glu Glu Gly Gly Gln Phe Val Thr Leu Ser Pro Pro  
 290 295 300

Cys Pro Glu Phe Pro Tyr Glu Ile Asn Tyr  
 305 310

<210> 25

<211> 702

<212> DNA

<213> Type B PWD circovirus

<220>

<221> CDS

<222> (1)..(699)

<400> 25

atg acg tat cca agg agg cgt tac cga aga aga cac cgc ccc cgc 48  
 Met Thr Tyr Pro Arg Arg Arg Tyr Arg Arg Arg His Arg Pro Arg  
 1 5 10 15

agc cat ctt ggc cag atc ctc cgc cgc cgc ccc tgg ctc gtc cac ccc 96  
 Ser His Leu Gly Gln Ile Leu Arg Arg Arg Pro Trp Leu Val His Pro  
 20 25 30

cgc cac cgt tac cgc tgg aga agg aaa aat ggc atc ttc aac acc cgc 144  
 Arg His Arg Tyr Arg Trp Arg Arg Lys Asn Gly Ile Phe Asn Thr Arg  
 35 40 45

ctc tcc cgc acc ttc gga tat act gtc aag cga acc aca gtc aga acg 192  
 Leu Ser Arg Thr Phe Gly Tyr Thr Val Lys Arg Thr Thr Val Arg Thr  
 50 55 60

ccc tcc tgg gcg gtg gac atg atg aga ttc aat att aat gac ttt ctt 240  
 Pro Ser Trp Ala Val Asp Met Met Arg Phe Asn Ile Asn Asp Phe Leu  
 65 70 75 80

ccc cca gga ggg ggg tca aac ccc cgc tct gtg ccc ttt, gaa tac tac	288
Pro Pro Gly Gly Gly Ser Asn Pro Arg Ser Val Pro Phe Glu Tyr Tyr	
85 90 95	
aga ata aga aag gtt aag gtt gaa ttc tgg ccc tgc tcc ccg atc acc	336
Arg Ile Arg Lys Val Lys Val Glu Phe Trp Pro Cys Ser Pro Ile Thr	
100 105 110	
cag ggt gac agg gga gtg ggc tcc agt gct gtt att tta gat gat aac	384
Gln Gly Asp Arg Gly Val Gly Ser Ser Ala Val Ile Leu Asp Asp Asn	
115 120 125	
ttt gta aca aag gcc aca gcc ctc acc tat gac ccc tat gta aac tac	432
Phe Val Thr Lys Ala Thr Ala Leu Thr Tyr Asp Pro Tyr Val Asn Tyr	
130 135 140	
tcc tcc cgc cat acc ata acc cag ccc ttc tcc tac cac tcc cgg tac	480
Ser Ser Arg His Thr Ile Thr Gln Pro Phe Ser Tyr His Ser Arg Tyr	
145 150 155 160	
ttt acc ccc aaa cct gtc cta gat ttc act att gat tac ttc caa cca	528
Phe Thr Pro Lys Pro Val Leu Asp Phe Thr Ile Asp Tyr Phe Gln Pro	
165 170 175	
aac aac aaa aga aac cag ctg tgg ctg aga cta caa act gct gga aat	576
Asn Asn Lys Arg Asn Gln Leu Trp Leu Arg Leu Gln Thr Ala Gly Asn	
180 185 190	
gta gac cac gta ggc ctc ggc act gcg ttc gaa aac agt ata tac gac	624
Val Asp His Val Gly Leu Gly Thr Ala Phe Glu Asn Ser Ile Tyr Asp	
195 200 205	
cag gaa tac aat atc cgt gta acc atg tat gta caa ttc aga gaa ttt	672
Gln Glu Tyr Asn Ile Arg Val Thr Met Tyr Val Gln Phe Arg Glu Phe	
210 215 220	
aat ttt aaa gac ccc cca ctt aac cct taa	702
Asn Phe Lys Asp Pro Pro Leu Asn Pro	
225 230	

<210> 26

<211> 233

<212> PRT

<213> Type B PWD circovirus

<400> 26



Met Thr Tyr Pro Arg Arg Arg Tyr Arg Arg Arg Arg His Arg Pro Arg  
1 5 10 15

Ser His Leu Gly Gln Ile Leu Arg Arg Arg Pro Trp Leu Val His Pro  
20 25 30

Arg His Arg Tyr Arg Trp Arg Arg Lys Asn Gly Ile Phe Asn Thr Arg  
35 40 45

Leu Ser Arg Thr Phe Gly Tyr Thr Val Lys Arg Thr Thr Val Arg Thr  
50 55 60

Pro Ser Trp Ala Val Asp Met Met Arg Phe Asn Ile Asn Asp Phe Leu  
65 70 75 80

Pro Pro Gly Gly Gly Ser Asn Pro Arg Ser Val Pro Phe Glu Tyr Tyr  
85 90 95

Arg Ile Arg Lys Val Lys Val Glu Phe Trp Pro Cys Ser Pro Ile Thr  
100 105 110

Gln Gly Asp Arg Gly Val Gly Ser Ser Ala Val Ile Leu Asp Asp Asn  
115 120 125

Phe Val Thr Lys Ala Thr Ala Leu Thr Tyr Asp Pro Tyr Val Asn Tyr  
130 135 140

Ser Ser Arg His Thr Ile Thr Gln Pro Phe Ser Tyr His Ser Arg Tyr  
145 150 155 160

Phe Thr Pro Lys Pro Val Leu Asp Phe Thr Ile Asp Tyr Phe Gln Pro  
165 170 175

Asn Asn Lys Arg Asn Gln Leu Trp Leu Arg Leu Gln Thr Ala Gly Asn  
180 185 190

Val Asp His Val Gly Leu Gly Thr Ala Phe Glu Asn Ser Ile Tyr Asp  
195 200 205

Gln Glu Tyr Asn Ile Arg Val Thr Met Tyr Val Gln Phe Arg Glu Phe  
210 215 220

Asn Phe Lys Asp Pro Pro Leu Asn Pro  
225 230

<210> 27

<211> 315

<212> DNA

<213> Type B PWD circovirus

<220>

<221> CDS

<222> (1)..(312)

<400> 27

atg gta acc atc cca cca ctt gtt tct agg tgg ttt cca gta tgt ggt	48
Met Val Thr Ile Pro Pro Leu Val Ser Arg Trp Phe Pro Val Cys Gly	
1 5 10 15	

ttc cgg gtc tgc aaa att agc agc cca ttt gct ttt acc aca ccc agg	96
Phe Arg Val Cys Lys Ile Ser Ser Pro Phe Ala Phe Thr Thr Pro Arg	
20 25 30	

tgg ccc cac aat gac gtg tac att agt ctt cca atc acg ctt ctg cat	144
Trp Pro His Asn Asp Val Tyr Ile Ser Leu Pro Ile Thr Leu Leu His	
35 40 45	

ttt ccc gct cac ttt caa aag ttc agc cag ccc gcg gaa att tct gac	192
Phe Pro Ala His Phe Gln Lys Phe Ser Gln Pro Ala Glu Ile Ser Asp	
50 55 60	

aaa cgt tac agg gtg ctg ctc tgc aac ggt cac cag act ccc gct ctc	240
Lys Arg Tyr Arg Val Leu Leu Cys Asn Gly His Gln Thr Pro Ala Leu	
65 70 75 80	

caa caa ggt act cac agc agt aga cag gtc act ccg ttg tcc ctg aga	288
Gln Gln Gly Thr His Ser Ser Arg Gln Val Thr Pro Leu Ser Leu Arg	
85 90 95	

tct agg agc tcc aca ctc cat cag taa	315
Ser Arg Ser Ser Thr Leu His Gln	
100	

<210> 28

<211> 104

<212> PRT

<213> Type B PWD circovirus

<400> 28

Met Val Thr Ile Pro Pro Leu Val Ser Arg Trp Phe Pro Val Cys Gly  
1 5 10 15

Phe Arg Val Cys Lys Ile Ser Ser Pro Phe Ala Phe Thr Thr Pro Arg  
20 25 30

Trp Pro His Asn Asp Val Tyr Ile Ser Leu Pro Ile Thr Leu Leu His  
35 40 45

Phe Pro Ala His Phe Gln Lys Phe Ser Gln Pro Ala Glu Ile Ser Asp  
50 55 60

Lys Arg Tyr Arg Val Leu Leu Cys Asn Gly His Gln Thr Pro Ala Leu  
65 70 75 80

Gln Gln Gly Thr His Ser Ser Arg Gln Val Thr Pro Leu Ser Leu Arg  
85 90 95

Ser Arg Ser Ser Thr Leu His Gln  
100

<210> 29

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 29

Val Asp Met Met Arg Phe Asn Ile Asn Asp Phe Leu Pro Pro Gly  
1 5 10 15

<210> 30

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 30

Gln	Gly	Asp	Arg	Gly	Val	Gly	Ser	Ser	Ala	Val	Ile	Leu	Asp	Asp
1				5					10					15

<210> 31

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 31

Gly	Val	Gly	Ser	Ser	Ala	Val	Ile	Leu	Asp	Asp	Asn	Phe	Val	Thr
1				5					10					15

<210> 32

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 32

Val	Asp	His	Val	Gly	Leu	Gly	Thr	Ala	Phe	Glu	Asn	Ser	Ile	Tyr
1				5					10					15

<210> 33

<211> 8

<212> DNA

<213> Type A PWD circovirus

<400> 33

tgtggcga

8

145

<210> 34

<211> 8

<212> DNA

<213> Type A PWD circovirus

<400> 34  
agttttcct

8

<210> 35

<211> 20

<212> DNA

<213> Type A PWD circovirus

<400> 35  
tcatttagag ggtctttcag

20

<210> 36

<211> 8

<212> DNA

<213> Type A PWD circovirus

<400> 36  
gtcaacct

8

<210> 37

<211> 8

<212> DNA

<213> Type A PWD circovirus

<400> 37  
gtgggttgc

8

<210> 38

<211> 8

<212> DNA

<213> Type A PWD circovirus

<400> 38

agcccagg

8

<210> 39

<211> 8

<212> DNA

<213> Type A PWD circovirus

<400> 39

ttggctgg

8

<210> 40

<211> 12

<212> DNA

<213> Type A PWD circovirus

<400> 40

tctagctctg gt

12

<210> 41

<211> 12

<212> DNA

<213> Type A PWD circovirus

<400> 41

atctcagctc gt

12

<210> 42

<211> 12

<212> DNA

<213> Type A PWD circovirus

<400> 42

tgtcctcctc tt

12

<210> 43

<211> 8

<212> DNA

<213> Type A PWD circovirus

<400> 43

tctctaga

8

<210> 44

<211> 8

<212> DNA

<213> Type A PWD circovirus

<400> 44

tgtaccaa

8

<210> 45

<211> 8

<212> DNA

<213> Type A PWD circovirus

<400> 45

tccgtctt

8

<210> 46

<211> 20

<212> DNA

<213> Primer

<400> 46

gtgtgctcga cattggtgtg

20

<210> 47

<211> 20

<212> DNA

<213> Primer

<400> 47

tggaaatgtta acgagctgag

20

<210> 48

<211> 20

<212> DNA

<213> Primer

<400> 48

ctcgcagcca tcttggaatg

20

<210> 49

<211> 20

<212> DNA

<213> Primer

<400> 49

cgcgcgtaat acgactcact

20



<210> 50

<211> 26

<212> DNA

<213> Primer

<400> 50

cctgtctact gctgtgagta ccttgt

26

<210> 51

<211> 26

<212> DNA

<213> Primer

<400> 51

gcagtagaca ggtcactccg ttgtcc

26

<210> 52

<211> 20

<212> DNA

<213> Primer

<400> 52

tggaatgtta actacctcaa

20

<210> 53

<211> 23

<212> DNA

<213> Primer

<400> 53

ggcggcgcca tctgtaacgg ttt

23

<210> 54

<211> 23

<212> DNA

<213> Primer

<400> 54

gatggcgccg aaagacgggt atc

23

<210> 55

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 55

Asn	Val	Asn	Glu	Leu	Arg	Phe	Asn	Ile	Gly	Gln	Phe	Leu	Pro	Pro
1				5					10				15	

<210> 56

<211> 14

<212> PRT

<213> Type A PWD circovirus

<400> 56

Thr	Ser	Asn	Gln	Arg	Gly	Val	Gly	Ser	Thr	Val	Val	Ile	Leu
1				5				10					

<210> 57

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 57

Arg Gly Val Gly Ser Thr Val Val Ile Leu Asp Ala Asn Phe Val  
1 5 10 15

<210> 58

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 58

Phe Thr Ile Asp Tyr Phe Gln Pro Asn Asn Lys Arg Asn Gln Leu  
1 5 10 15

<210> 59

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 59

Asp Gln Thr Ile Asp Trp Phe Gln Pro Asn Asn Lys Arg Asn Gln  
1 5 10 15

<210> 60

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 60

Asn Val Glu His Thr Gly Leu Gly Tyr Ala Leu Gln Asn Ala Thr  
1 5 10 15

<210> 61

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 61

His Arg Pro Arg Ser His Leu Gly Gln Ile Leu Arg Arg Arg Pro  
1 5 10 15

<210> 62

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 62

Ser His Leu Gly Gln Ile Leu Arg Arg Arg Pro Trp Leu Val His  
1 5 10 15

<210> 63

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 63

Gln Ile Leu Arg Arg Arg Pro Trp Leu Val His Pro Arg His Arg  
1 5 10 15

<210> 64

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 64

Arg Arg Pro Trp Leu Val His Pro Arg His Arg Tyr Arg Trp Arg  
1 5 10 15

<210> 65

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 65

Leu	Val	His	Pro	Arg	His	Arg	Tyr	Arg	Trp	Arg	Arg	Lys	Asn	Gly
1			5						10					15

<210> 66

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 66

Arg	His	Arg	Tyr	Arg	Trp	Arg	Arg	Lys	Asn	Gly	Ile	Phe	Asn	Thr
1				5					10					15

<210> 67

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 67

Arg	Trp	Arg	Arg	Lys	Asn	Gly	Ile	Phe	Asn	Thr	Arg	Leu	Ser	Arg
1				5					10					15

<210> 68

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 68

Lys	Asn	Gly	Ile	Phe	Asn	Thr	Arg	Leu	Ser	Arg	Thr	Phe	Gly	Tyr
1				5					10					15

<210> 69

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 69

Phe	Asn	Thr	Arg	Leu	Ser	Arg	Thr	Phe	Gly	Tyr	Thr	Val	Lys	Arg
1				5					10					15

<210> 70

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 70

Leu	Ser	Arg	Thr	Phe	Gly	Tyr	Thr	Val	Lys	Arg	Thr	Thr	Val	Arg
1				5					10					15

<210> 71

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 71

Phe	Gly	Tyr	Thr	Val	Lys	Arg	Thr	Thr	Val	Arg	Thr	Pro	Ser	Trp
1				5					10					15

<210> 72

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 72

Val	Lys	Arg	Thr	Thr	Val	Arg	Thr	Pro	Ser	Trp	Ala	Val	Asp	Met
1				5					10					15

<210> 73

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 73

Thr	Val	Arg	Thr	Pro	Ser	Trp	Ala	Val	Asp	Met	Met	Arg	Phe	Asn
1				5					10					15

<210> 74

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 74

Pro	Ser	Trp	Ala	Val	Asp	Met	Met	Arg	Phe	Asn	Ile	Asn	Asp	Phe
1				5					10					15

<210> 75

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 75

Arg	Phe	Asn	Ile	Asn	Asp	Phe	Leu	Pro	Pro	Gly	Gly	Gly	Ser	Asn
1				5					10					15

<210> 76

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 76

Asn Asp Phe Leu Pro Pro Gly Gly Gly Ser Asn Pro Arg Ser Val  
1 5 10 15

<210> 77

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 77

Pro Pro Gly Gly Gly Ser Asn Pro Arg Ser Val Pro Phe Glu Tyr  
1 5 10 15

<210> 78

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 78

Gly Ser Asn Pro Arg Ser Val Pro Phe Glu Tyr Tyr Arg Ile Arg  
1 5 10 15

<210> 79

<211> 15

<212> PRT

<213> Type B PWD circovirus



<400> 79

Arg	Ser	Val	Pro	Phe	Glu	Tyr	Tyr	Arg	Ile	Arg	Lys	Val	Lys	Val
1				5					10					15

<210> 80

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 80

Phe	Glu	Tyr	Tyr	Arg	Ile	Arg	Lys	Val	Lys	Val	Glu	Phe	Trp	Pro
1				5					10					15

<210> 81

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 81

Arg	Ile	Arg	Lys	Val	Lys	Val	Glu	Phe	Trp	Pro	Cys	Ser	Pro	Ile
1				5					10					15

<210> 82

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 82

Val	Lys	Val	Glu	Phe	Trp	Pro	Cys	Ser	Pro	Ile	Thr	Gln	Gly	Asp
1				5					10					15

<210> 83

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 83

Phe Trp Pro Cys Ser Pro Ile Thr Gln Gly Asp Arg Gly Val Gly  
1 5 10 15

<210> 84

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 84

Thr Arg Pro Arg Ser His Leu Gly Asn Ile Leu Arg Arg Arg Pro  
1 5 10 15

<210> 85

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 85

Ser His Leu Gly Asn Ile Leu Arg Arg Arg Pro Tyr Leu Val His  
1 5 10 15

<210> 86

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 86

Asn Ile Leu Arg Arg Arg Pro Tyr Leu Val His Pro Ala Phe Arg  
1 5 10 15

<210> 87

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 87

Arg	Arg	Pro	Tyr	Leu	Val	His	Pro	Ala	Phe	Arg	Asn	Arg	Tyr	Arg
1				5					10					15

<210> 88

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 88

Leu	Val	His	Pro	Ala	Phe	Arg	Asn	Arg	Tyr	Arg	Trp	Arg	Arg	Lys
1				5					10					15

<210> 89

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 89

Ala	Phe	Arg	Asn	Arg	Tyr	Arg	Trp	Arg	Arg	Lys	Thr	Gly	Ile	Phe
1				5					10					15

<210> 90

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 90

Arg	Tyr	Arg	Trp	Arg	Arg	Lys	Thr	Gly	Ile	Phe	Asn	Ser	Arg	Leu
1				5					10					15

<210> 91

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 91

Arg	Arg	Lys	Thr	Gly	Ile	Phe	Asn	Ser	Arg	Leu	Ser	Arg	Glu	Phe
1				5					10					15

<210> 92

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 92

Gly	Ile	Phe	Asn	Ser	Arg	Leu	Ser	Arg	Glu	Phe	Val	Leu	Thr	Ile
1				5					10					15

<210> 93

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 93

Ser	Arg	Leu	Ser	Arg	Glu	Phe	Val	Leu	Thr	Ile	Arg	Gly	Gly	His
1				5					10					15

<210> 94

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 94

Arg	Glu	Phe	Val	Leu	Thr	Ile	Arg	Gly	Gly	His	Ser	Gln	Pro	Ser
1				5					10					15

<210> 95

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 95

Leu	Thr	Ile	Arg	Gly	Gly	His	Ser	Gln	Pro	Ser	Trp	Asn	Val	Asn
1				5					10					15

<210> 96

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 96

Gly	Gly	His	Ser	Gln	Pro	Ser	Trp	Asn	Val	Asn	Glu	Leu	Arg	Phe
1				5					10					15

<210> 97

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 97

Gln	Pro	Ser	Trp	Asn	Val	Asn	Glu	Leu	Arg	Phe	Asn	Ile	Gly	Gln
1				5					10					15

<210> 98

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 98

Asn Val Asn Glu Leu Arg Phe Asn Ile Gly Gln Phe Leu Pro Pro  
1 5 10 15

<210> 99

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 99

Leu Arg Phe Asn Ile Gly Gln Phe Leu Pro Pro Ser Gly Gly Thr  
1 5 10 15

<210> 100

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 100

Ile Gly Gln Phe Leu Pro Pro Ser Gly Gly Thr Asn Pro Leu Pro  
1 5 10 15

<210> 101

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 101

Leu Pro Pro Ser Gly Gly Thr Asn Pro Leu Pro Leu Pro Phe Gln  
1 5 10 15

<210> 102

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 102

Gly Gly Thr Asn Pro Leu Pro Leu Pro Phe Gln Tyr Tyr Arg Ile  
1 5 10 15

<210> 103

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 103

Pro Leu Pro Leu Pro Phe Gln Tyr Tyr Arg Ile Arg Lys Ala Lys  
1 5 10 15

<210> 104

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 104

Pro Phe Gln Tyr Tyr Arg Ile Arg Lys Ala Lys Tyr Glu Phe Tyr  
1 5 10 15

<210> 105

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 105

Tyr	Arg	Ile	Arg	Lys	Ala	Lys	Tyr	Glu	Phe	Tyr	Pro	Arg	Asp	Pro
1				5				10					15	

<210> 106

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 106

Lys	Ala	Lys	Tyr	Glu	Phe	Tyr	Pro	Arg	Asp	Pro	Ile	Thr	Ser	Asn
1				5				10					15	

<210> 107

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 107

Glu	Phe	Tyr	Pro	Arg	Asp	Pro	Ile	Thr	Ser	Asn	Gln	Arg	Gly	Val
1				5				10					15	

<210> 108

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 108

Arg	Asp	Pro	Ile	Thr	Ser	Asn	Gln	Arg	Gly	Val	Gly	Ser	Thr	Val
1				5				10				15		



<210> 109

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 109

Thr	Ser	Asn	Gln	Arg	Gly	Val	Gly	Ser	Thr	Val	Val	Ile	Leu	Asp
1				5				10					15	

<210> 110

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 110

Gly	Val	Gly	Ser	Ser	Ala	Val	Ile	Leu	Asp	Asp	Asn	Phe	Val	Thr
1				5				10					15	

<210> 111

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 111

Ser	Ala	Val	Ile	Leu	Asp	Asp	Asn	Phe	Val	Thr	Lys	Ala	Thr	Ala
1				5				10					15	

<210> 112

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 112

Leu	Asp	Asp	Asn	Phe	Val	Thr	Lys	Ala	Thr	Ala	Leu	Thr	Tyr	Asp
1			5					10					15	

<210> 113

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 113

Phe	Val	Thr	Lys	Ala	Thr	Ala	Leu	Thr	Tyr	Asp	Pro	Tyr	Val	Asn
1			5					10					15	

<210> 114

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 114

Ala	Thr	Ala	Leu	Thr	Tyr	Asp	Pro	Tyr	Val	Asn	Tyr	Ser	Ser	Arg
1			5					10					15	

<210> 115

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 115

Thr	Tyr	Asp	Pro	Tyr	Val	Asn	Tyr	Ser	Ser	Arg	His	Thr	Ile	Thr
1			5					10					15	

<210> 116

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 116

Tyr	Val	Asn	Tyr	Ser	Ser	Arg	His	Thr	Ile	Thr	Gln	Pro	Phe	Ser
1				5					10					15

<210> 117

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 117

Ser	Ser	Arg	His	Thr	Ile	Thr	Gln	Pro	Phe	Ser	Tyr	His	Ser	Arg
1				5					10					15

<210> 118

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 118

Thr	Ile	Thr	Gln	Pro	Phe	Ser	Tyr	His	Ser	Arg	Tyr	Phe	Thr	Pro
1				5					10					15

<210> 119

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 119

Pro	Phe	Ser	Tyr	His	Ser	Arg	Tyr	Phe	Thr	Pro	Lys	Pro	Val	Leu
1				5					10					15

<210> 120

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 120

His	Ser	Arg	Tyr	Phe	Thr	Pro	Lys	Pro	Val	Leu	Asp	Phe	Thr	Ile
1				5					10					15

<210> 121

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 121

Phe	Thr	Pro	Lys	Pro	Val	Leu	Asp	Phe	Thr	Ile	Asp	Tyr	Phe	Gln
1				5					10					15

<210> 122

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 122

Pro	Val	Leu	Asp	Phe	Thr	Ile	Asp	Tyr	Phe	Gln	Pro	Asn	Asn	Lys
1				5					10					15

<210> 123

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 123

Phe Thr Ile Asp Tyr Phe Gln Pro Asn Asn Lys Arg Asn Gln Leu  
1 5 10 15

<210> 124

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 124

Tyr Phe Gln Pro Asn Asn Lys Arg Asn Gln Leu Trp Leu Arg Leu  
1 5 10 15

<210> 125

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 125

Asn Asn Lys Arg Asn Gln Leu Trp Leu Arg Leu Gln Thr Ala Gly  
1 5 10 15

<210> 126

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 126

Asn Gln Leu Trp Leu Arg Leu Gln Thr Ala Gly Asn Val Asp His  
1 5 10 15

<210> 127

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 127

Leu	Arg	Leu	Gln	Thr	Ala	Gly	Asn	Val	Asp	His	Val	Gly	Leu	Gly
1				5					10					15

<210> 128

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 128

Thr	Ala	Gly	Asn	Val	Asp	His	Val	Gly	Leu	Gly	Thr	Ala	Phe	Glu
1				5					10					15

<210> 129

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 129

Gly	Leu	Gly	Thr	Ala	Phe	Glu	Asn	Ser	Ile	Tyr	Asp	Gln	Glu	Tyr
1				5					10					15

<210> 130

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 130

Ala	Phe	Glu	Asn	Ser	Ile	Tyr	Asp	Gln	Glu	Tyr	Asn	Ile	Arg	Val
1				5					10					15

<210> 131

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 131

Ser	Ile	Tyr	Asp	Gln	Glu	Tyr	Asn	Ile	Arg	Val	Thr	Met	Tyr	Val
1				5					10					15

<210> 132

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 132

Gln	Glu	Tyr	Asn	Ile	Arg	Val	Thr	Met	Tyr	Val	Gln	Phe	Arg	Glu
1				5					10					15

<210> 133

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 133

Ile	Arg	Val	Thr	Met	Tyr	Val	Gln	Phe	Arg	Glu	Phe	Asn	Phe	Lys
1				5					10					15

<210> 134

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 134

Met Tyr Val Gln Phe Arg Glu Phe Asn Phe Lys Asp Pro Pro Leu  
1 5 10 15

<210> 135

<211> 15

<212> PRT

<213> Type B PWD circovirus

<400> 135

Val Gln Phe Arg Glu Phe Asn Phe Lys Asp Pro Pro Leu Asn Pro  
1 5 10 15

<210> 136

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 136

Arg Gly Val Gly Ser Thr Val Val Ile Leu Asp Ala Asn Phe Val  
1 5 10 15

<210> 137

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 137

Ser Thr Val Val Ile Leu Asp Ala Asn Phe Val Thr Pro Ser Thr  
1 5 10 15

<210> 138

<211> 15

<212> PRT



<213> Type A PWD circovirus

<400> 138

Ile	Leu	Asp	Ala	Asn	Phe	Val	Thr	Pro	Ser	Thr	Asn	Leu	Ala	Tyr
1				5					10					15

<210> 139

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 139

Asn	Phe	Val	Thr	Pro	Ser	Thr	Asn	Leu	Ala	Tyr	Asp	Pro	Tyr	Ile
1				5					10					15

<210> 140

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 140

Pro	Ser	Thr	Asn	Leu	Ala	Tyr	Asp	Pro	Tyr	Ile	Asn	Tyr	Ser	Ser
1				5					10					15

<210> 141

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 141

Leu	Ala	Tyr	Asp	Pro	Tyr	Ile	Asn	Tyr	Ser	Ser	Arg	His	Thr	Ile
1				5					10					15

<210> 142

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 142

Pro	Tyr	Ile	Asn	Tyr	Ser	Ser	Arg	His	Thr	Ile	Arg	Gln	Pro	Phe
1				5					10					15

<210> 143

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 143

Tyr	Ser	Ser	Arg	His	Thr	Ile	Arg	Gln	Pro	Phe	Thr	Tyr	His	Ser
1				5					10					15

<210> 144

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 144

His	Thr	Ile	Arg	Gln	Pro	Phe	Thr	Tyr	His	Ser	Arg	Tyr	Phe	Thr
1				5					10					15

<210> 145

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 145

Gln Pro Phe Thr Tyr His Ser Arg Tyr Phe Thr Pro Lys Pro Glu  
1 5 10 15

<210> 146

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 146

Tyr His Ser Arg Tyr Phe Thr Pro Lys Pro Glu Leu Asp Gln Thr  
1 5 10 15

<210> 147

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 147

Tyr Phe Thr Pro Lys Pro Glu Leu Asp Gln Thr Ile Asp Trp Phe  
1 5 10 15

<210> 148

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 148

Lys Pro Glu Leu Asp Gln Thr Ile Asp Trp Phe Gln Pro Asn Asn  
1 5 10 15

<210> 149

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 149

Asp	Gln	Thr	Ile	Asp	Trp	Phe	Gln	Pro	Asn	Asn	Lys	Arg	Asn	Gln
1				5					10					15

<210> 150

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 150

Asp	Trp	Phe	Gln	Pro	Asn	Asn	Lys	Arg	Asn	Gln	Leu	Trp	Leu	His
1				5					10					15

<210> 151

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 151

Pro	Asn	Asn	Lys	Arg	Asn	Gln	Leu	Trp	Leu	His	Leu	Asn	Thr	His
1				5					10					15

<210> 152

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 152

Arg	Asn	Gln	Leu	Trp	Leu	His	Leu	Asn	Thr	His	Thr	Asn	Val	Glu
1				5					10					15

<210> 153

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 153

Trp	Leu	His	Leu	Asn	Thr	His	Thr	Asn	Val	Glu	His	Thr	Gly	Leu
1				5					10					15

<210> 154

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 154

Asn	Thr	His	Thr	Asn	Val	Glu	His	Thr	Gly	Leu	Gly	Tyr	Ala	Leu
1				5					10					15

<210> 155

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 155

Asn	Val	Glu	His	Thr	Gly	Leu	Gly	Tyr	Ala	Leu	Gln	Asn	Ala	Thr
1				5					10					15

<210> 156

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 156

Thr Gly Leu Gly Tyr Ala Leu Gln Asn Ala Thr Thr Ala Gln Asn  
1 5 10 15

<210> 157

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 157

Tyr Ala Leu Gln Asn Ala Thr Thr Ala Gln Asn Tyr Val Val Arg  
1 5 10 15

<210> 158

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 158

Asn Ala Thr Thr Ala Gln Asn Tyr Val Val Arg Leu Thr Ile Tyr  
1 5 10 15

<210> 159

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 159

Ala Gln Asn Tyr Val Val Arg Leu Thr Ile Tyr Val Gln Phe Arg  
1 5 10 15

<210> 160

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 160

Val Val Arg Leu Thr Ile Tyr Val Gln Phe Arg Glu Phe Ile Leu  
1 5 10 15

<210> 161

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 161

Thr Ile Tyr Val Gln Phe Arg Glu Phe Ile Leu Lys Asp Pro Leu  
1 5 10 15

<210> 162

<211> 15

<212> PRT

<213> Type A PWD circovirus

<400> 162

Tyr Val Gln Phe Arg Glu Phe Ile Leu Lys Asp Pro Leu Asn Glu  
1 5 10 15

<210> 163

<211> 1759

<212> DNA

<213> Type A PWD circovirus

<400> 163

accagcgcac ttcggcagcg gcagcacctc ggcagcgtca gtgaaaatgc caagcaagaa 60  
aagcggcccg caaccccata agaggtgggt gttcaccctt aataatcctt ccgaggagga 120

gaaaaacaaa atacgggagc ttccaatctc cctttttgat ttttttgttt gcggagagga	180
aggttttgaa gagggtagaa ctctcacct ccaggggttt gcgaattttg ctaagaagca	240
gacttttaac aaggtgaagt ggtatttttg tgcccgtgc cacatcgaga aagcgaaagg	300
aaccgaccag cagaataaag aatactgcag taaagaaggc cacatactta tcgagtgtgg	360
agctccgcgg aaccagggga agcgcagcga cctgtctact gctgtgagta cccttttgga	420
gacggggtct ttggtgactg tagccgagca gttccctgta acgtatgtga gaaatttccg	480
cgggctggct gaacttttga aagtgcgcgg gaagatgcag aagcgtgatt ggaagacagc	540
tgtacacgtc atagtgggcc cgcccgttg tgggaagagc cagtggggcc gtaattttgc	600
tgagcctagg gacacctact ggaagcctag tagaaataag tgggtgggatg gatatcatgg	660
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actgtgtgac cggtatccat tgactgtaga gactaaaggg ggtactgttc cttttttggc	780
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agaacaatcc acggaggtac ccgaaggccg atttgaagca gtggaccac cctgtgccct	960
tttcccatat aaaataaatt actgagctct tttgtttatc acatcgtaat ggtttttatt	1020
tttattttatt tagagggtct tttaggataa attctctgaa ttgtacataa atagtcagcc	1080
ttaccacata attttgggct gtggttgcac tttggagcgc atagcccagg cctgtgtgct	1140
cgacattggt gtgggtatct aaatggagcc acagctggtt tcttttatta tttgggtgga	1200
accaatcaat tgtttgggcc agctcagggt tgggggtgaa gtacctggag tggtaggtaa	1260
agggctgcct tatggtgtgg cgggaggagt agttaatata ggggtcatag gccaagtgg	1320
tggaggggggt taaaaagttg gcatccaaga taacaacagt ggaccaaca cctctttgat	1380
tagagggtgat ggggtctctg gggtaaaatt catatttagc ctttctaata cggtagtatt	1440
ggaaaggtag gggtaggggg ttggtgccgc ctgagggggg gaggaactgg ccgatgttga	1500
atttcagcta gttaacattc caagatggct gcgagtatcc tccttttatg gtgagtacaa	1560
attctgtaga aaggcgggaa ttgaagatac ccgtctttcg gcgccatctg taacggtttc	1620
tgaaggcggg gtgtgccaaa tatggtcttc tccgaggat gtttccaaga tggctgcggg	1680
ggcgggtcct tcttctgcgg taacgcctcc ttggccacgt catcctataa aagtgaagaa	1740
agtgcgctgc ttagtagtatt	1759



<210> 164

<211> 1759

<212> DNA

<213> Type A PWD circovirus

<400> 164

accagcgcac	ttcggcagcg	gcagcacctc	ggcagcgtca	gtgaaaatgc	caagcaagaa	60
aagcggcccg	caaccccata	agaggtgggt	gttcaccctt	aataatcctt	ccgaggagga	120
gaaaaacaaa	atacgggagc	ttccaatctc	cctttttgat	tattttgttt	gcgagagga	180
aggtttggaa	gagggtagaa	ctcctcacct	ccaggggttt	gctaattttg	ctaagaagca	240
gacttttaac	aaggtgaagt	ggtatttttg	tgcccgtgc	cacatcgaga	aagcgaaagg	300
aaccgaccag	cagaataaag	aatactgcag	taaagaaggc	cacatactta	tcgagtgtgg	360
agctccgchg	aaccagggga	agcgcagcga	cctgtctact	gctgtgagta	cccttttggg	420
gacggggctc	ttggtgactg	tagccgagca	gttccctgta	acgtatgtga	gaaatttccg	480
cgggctggct	gaacttttga	aagtgagcgg	gaagatgcag	aagcgtgatt	ggaagacagc	540
tgtacacgtc	atagtggggc	cgcccgggtg	tgggaagagc	cagtggggcc	gtaattttgc	600
tgagcctagc	gacacctact	ggaagcctag	tagaaataag	tggtgggatg	gatatcatgg	660
agaagaagtt	gttgtttttg	atgattttta	tggctgggta	ccttgggatg	atctactgag	720
actgtgtgac	cggtatccat	tgactgtaga	gactaaaggc	ggtactgttc	cttttttggc	780
tcgcagtatt	ttgattacca	gcaatcaggc	ccccaggaa	tggtactcct	caactgctgt	840
cccagctgta	gaagctctct	atcggaggat	tactactttg	caattttgga	agactgctgg	900
agaacaatca	acggaggtac	ccgaaggccg	atttgaagca	gtggaccac	cctgtgccct	960
tttcccatat	aaaataaatt	actgagtctt	ttttgttata	acatcgtaat	ggtttttatt	1020
tttattttatt	tagagggtct	tttaggataa	attctctgaa	ttgtacataa	atagtcagcc	1080
ttaccacata	attttgggct	gtgggttgc	tttgagcgc	atagcccagg	cctgtgtgct	1140
cgacattggt	gtgggtat	aaatggagcc	acagctgggt	tcttttatta	tttgggtgga	1200
accattcaat	tgtttgggtc	agctcagggt	tgggggtgaa	gtacctggag	tggtaggtaa	1260

agggctgcct tatggtgtgg cgggaggagt agttaatata ggggtcatag gccaaagtgg 1320  
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 ggaaaggtag gggtaggggg ttggtgccgc ctgagggggg gaggaactgg cccatgttga 1500  
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 tgaaggcggg gtgtgccaaa tatggtcttc tccggaggat gttccaaga tggctgcggg 1680  
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 agtgcgctgc tgtagtatt 1759

<210> 165

<211> 312

<212> PRT

<213> Type A PWD circovirus

<400> 165

Met	Pro	Ser	Lys	Lys	Ser	Gly	Pro	Gln	Pro	His	Lys	Arg	Trp	Val	Phe
1				5					10					15	
Thr	Leu	Asn	Asn	Pro	Ser	Gly	Gly	Gly	Lys	Asn	Lys	Ile	Arg	Gly	Leu
			20					25					30		
Pro	Ile	Ser	Leu	Phe	Asp	Tyr	Phe	Val	Cys	Gly	Gly	Gly	Gly	Leu	Gly
		35					40					45			
Gly	Gly	Arg	Thr	Pro	His	Leu	Gln	Gly	Phe	Ala	Asn	Phe	Ala	Lys	Lys
	50					55					60				
Gln	Thr	Phe	Asn	Lys	Val	Lys	Trp	Tyr	Phe	Gly	Ala	Arg	Cys	His	Ile
65					70					75				80	
Gly	Lys	Ala	Lys	Gly	Thr	Asp	Gln	Gln	Asn	Lys	Gly	Tyr	Cys	Ser	Lys
				85					90					95	
Gly	Gly	His	Ile	Leu	Ile	Gly	Cys	Gly	Ala	Pro	Arg	Asn	Gln	Gly	Lys
			100					105					110		
Arg	Ser	Asp	Leu	Ser	Thr	Ala	Val	Ser	Thr	Leu	Leu	Gly	Thr	Gly	Ser
		115					120					125			

Leu Val Thr Val Ala Gly Gln Phe Pro Val Thr Tyr Val Arg Asn Phe  
130 135 140

Arg Gly Leu Ala Gly Leu Leu Lys Val Ser Gly Lys Met Gln Gln Arg  
145 150 155 160

Asp Trp Lys Thr Ala Val His Val Ile Val Gly Pro Pro Gly Cys Gly  
165 170 175

Lys Ser Gln Trp Ala Arg Asn Phe Ala Gly Pro Arg Asp Thr Tyr Trp  
180 185 190

Lys Pro Ser Arg Asn Lys Trp Trp Asp Gly Tyr His Gly Gly Gly Val  
195 200 205

Val Val Leu Asp Asp Phe Tyr Gly Trp Leu Pro Trp Asp Asp Leu Leu  
210 215 220

Arg Leu Cys Asp Arg Tyr Pro Leu Thr Val Gly Thr Lys Gly Gly Thr  
225 230 235 240

Val Pro Phe Leu Ala Arg Ser Ile Leu Ile Thr Ser Asn Gln Ala Pro  
245 250 255

Gln Gly Trp Tyr Ser Ser Thr Ala Val Pro Ala Val Gly Ala Leu Tyr  
260 265 270

Arg Arg Ile Thr Thr Leu Gln Phe Trp Lys Thr Ala Gly Gly Gln Ser  
275 280 285

Thr Gly Val Pro Gly Gly Arg Phe Gly Ala Val Asp Pro Pro Cys Ala  
290 295 300

Leu Phe Pro Tyr Lys Ile Asn Tyr  
305 310

<210> 166

<211> 312

<212> PRT

<213> Type A PWD circovirus

<400> 166

Met Pro Ser Lys Lys Ser Gly Pro Gln Pro His Lys Arg Trp Val Phe  
1 5 10 15

Thr Leu Asn Asn Pro Ser Gly Gly Gly Lys Asn Lys Ile Arg Gly Leu  
20 25 30

Pro Ile Ser Leu Phe Asp Tyr Phe Val Cys Gly Gly Gly Gly Leu Gly  
 35 40 45  
 Gly Gly Arg Thr Ala His Leu Gln Gly Phe Ala Asn Phe Ala Lys Lys  
 50 55 60  
 Gln Thr Phe Asn Lys Val Lys Trp Tyr Phe Gly Ala Arg Cys His Ile  
 65 70 75 80  
 Gly Lys Ala Lys Gly Thr Asp Gln Gln Asn Lys Gly Tyr Cys Ser Lys  
 85 90 95  
 Gly Gly His Ile Leu Ile Gly Cys Gly Ala Pro Arg Asn Gln Gly Lys  
 100 105 110  
 Arg Ser Asp Leu Ser Thr Ala Val Ser Thr Leu Leu Gly Thr Gly Ser  
 115 120 125  
 Leu Val Thr Val Ala Gly Gln Phe Pro Val Thr Tyr Val Arg Asn Phe  
 130 135 140  
 Arg Gly Leu Ala Gly Leu Leu Lys Val Ser Gly Lys Met Gln Gln Arg  
 145 150 155 160  
 Asp Trp Lys Thr Ala Val His Val Ile Val Gly Pro Pro Gly Cys Gly  
 165 170 175  
 Lys Ser Gln Trp Ala Arg Asn Phe Ala Gly Pro Ser Asp Thr Tyr Trp  
 180 185 190  
 Lys Pro Ser Arg Asn Lys Trp Trp Asp Gly Tyr His Gly Gly Gly Val  
 195 200 205  
 Val Val Leu Asp Asp Phe Tyr Gly Trp Leu Pro Trp Asp Asp Leu Leu  
 210 215 220  
 Arg Leu Cys Asp Arg Tyr Pro Leu Thr Val Gly Thr Lys Gly Gly Thr  
 225 230 235 240  
 Val Pro Phe Leu Ala Arg Ser Ile Leu Ile Thr Ser Asn Gln Ala Pro  
 245 250 255  
 Gln Gly Trp Tyr Ser Ser Thr Ala Val Pro Ala Val Gly Ala Leu Tyr  
 260 265 270  
 Arg Arg Ile Thr Thr Leu Gln Phe Trp Lys Thr Ala Gly Gly Gln Ser  
 275 280 285  
 Thr Gly Val Pro Gly Gly Arg Phe Gly Ala Val Asp Pro Pro Cys Ala  
 290 295 300  
 Leu Phe Pro Tyr Lys Ile Asn Tyr  
 305 310  
 <210> 167

<211> 233

<212> PRT

<213> Type A PWD circovirus

<400> 167

Met Thr Trp Pro Arg Arg Arg Tyr Arg Arg Arg Thr Arg Pro Arg  
1 5 10 15  
Ser His Leu Gly Asn Ile Leu Arg Arg Arg Pro Tyr Leu Ala His Pro  
20 25 30  
Ala Phe Arg Asn Arg Tyr Arg Trp Arg Arg Lys Thr Gly Ile Phe Asn  
35 40 45  
Ser Arg Leu Ser Thr Glu Phe Val Leu Thr Ile Arg Gly Gly His Ser  
50 55 60  
Gln Pro Ser Trp Asn Val Asn Tyr Leu Lys Phe Asn Ile Gly Gln Phe  
65 70 75 80  
Leu Pro Pro Ser Gly Gly Thr Asn Pro Leu Pro Leu Pro Phe Gln Tyr  
85 90 95  
Tyr Arg Ile Arg Lys Ala Lys Tyr Glu Phe Tyr Pro Arg Asp Pro Ile  
100 105 110  
Thr Ser Asn Gln Arg Gly Val Gly Ser Thr Val Val Ile Leu Asp Ala  
115 120 125  
Asn Phe Val Thr Pro Ser Thr Asn Leu Ala Tyr Asp Pro Tyr Ile Asn  
130 135 140  
Tyr Ser Ser Arg His Thr Ile Arg Gln Pro Phe Thr Tyr His Ser Arg  
145 150 155 160  
Tyr Phe Thr Pro Lys Pro Glu Leu Asp Gln Thr Ile Asp Trp Phe His  
165 170 175  
Pro Asn Asn Lys Arg Asn Gln Leu Trp Leu His Leu Asn Thr His Thr  
180 185 190  
Asn Val Glu His Thr Gly Leu Gly Tyr Ala Leu Gln Asn Ala Ala Thr  
195 200 205  
Ala Gln Asn Tyr Val Val Arg Leu Thr Ile Tyr Val Gln Phe Arg Glu  
210 215 220  
Phe Ile Leu Lys Asp Pro Leu Asn Lys  
225 230

<210> 168

<211> 233

<212> PRT

<213> Type A PWD circovirus

<400> 168

Met Thr Trp Pro Arg Arg Arg Tyr Arg Arg Arg Arg Thr Arg Pro Arg  
1 5 10 15  
Ser His Leu Gly Asn Ile Leu Arg Arg Arg Pro Tyr Leu Val His Pro  
20 25 30  
Ala Phe Arg Asn Arg Tyr Arg Trp Arg Arg Lys Thr Gly Ile Phe Asn  
35 40 45  
Cys Arg Leu Ser Lys Glu Phe Val Ile Thr Ile Arg Gly Gly His Ser  
50 55 60  
Gln Pro Ser Trp Ile Val Asn Ile Leu Arg Phe Asn Ile Gly Gln Phe  
65 70 75 80  
Leu Pro Pro Ser Gly Gly Thr Asn Pro Leu Pro Leu Pro Phe Gln Tyr  
85 90 95  
Tyr Arg Ile Arg Lys Ala Lys Tyr Glu Phe Tyr Pro Arg Asp Pro Ile  
100 105 110  
Thr Ser Asn Glu Arg Gly Val Gly Ser Thr Val Val Ile Leu Asp Ala  
115 120 125  
Asn Phe Val Thr Pro Ser Thr Asn Leu Ala Tyr Asp Pro Tyr Ile Asn  
130 135 140  
Tyr Ser Ser Arg His Thr Ile Arg Gln Pro Phe Thr Tyr His Ser Arg  
145 150 155 160  
Tyr Phe Thr Pro Lys Pro Glu Leu Asp Gln Thr Ile Glu Trp Phe His  
165 170 175  
Pro Asn Asn Lys Arg Asn Gln Leu Trp Leu His Leu Asn Thr His Thr  
180 185 190  
Asn Val Glu His Thr Gly Leu Gly Tyr Ala Leu Gln Asn Ala Ala Thr  
195 200 205  
Ala Gln Asn Tyr Val Val Arg Leu Thr Ile Tyr Val Gln Phe Arg Glu  
210 215 220

187

Phe Ile Leu Lys Asp Pro Leu Asn Lys  
225 230

<210> 169

<211> 206

<212> PRT

<213> Type A PWD circovirus

<400> 169

Met Ile Ser Ile Pro Pro Leu Ile Ser Thr Arg Leu Pro Val Gly Val  
1 5 10 15

Pro Arg Leu Ser Lys Ile Thr Gly Pro Leu Ala Leu Pro Thr Thr Gly  
20 25 30

Arg Ala His Tyr Asp Val Tyr Ser Cys Leu Pro Ile Thr Leu Leu His  
35 40 45

Leu Pro Ala His Phe Gln Lys Phe Ser Gln Pro Ala Glu Ile Ser His  
50 55 60

Ile Arg Tyr Arg Glu Leu Leu Gly Tyr Ser His Gln Arg Pro Arg Leu  
65 70 75 80

Gln Lys Gly Thr His Ser Ser Arg Gln Val Ala Ala Leu Pro Leu Val  
85 90 95

Pro Arg Ser Ser Thr Leu Asp Lys Tyr Val Ala Phe Phe Thr Ala Val  
100 105 110

Phe Phe Ile Leu Leu Val Gly Ser Phe Arg Phe Leu Asp Val Ala Ala  
115 120 125

Gly Thr Lys Ile Pro Leu His Leu Val Lys Ser Leu Leu Leu Ser Lys  
130 135 140

Ile Arg Lys Pro Leu Glu Val Arg Ser Ser Thr Leu Phe Gln Thr Phe  
145 150 155 160

Leu Ser Ala Asn Lys Ile Ile Lys Lys Gly Asp Trp Lys Leu Pro Tyr  
165 170 175

Phe Val Phe Leu Leu Leu Gly Arg Ile Ile Lys Gly Glu His Pro Pro  
180 185 190

Leu Met Gly Leu Arg Ala Ala Phe Leu Ala Trp His Phe His  
195 200 205

<210> 170

<211> 206

<212> PRT

<213> Type A PWD circovirus

<400> 170

Met	Ile	Ser	Ile	Pro	Pro	Leu	Ile	Ser	Thr	Arg	Leu	Pro	Val	Gly	Val
1				5					10					15	
Ala	Arg	Leu	Ser	Lys	Ile	Thr	Gly	Pro	Leu	Ala	Leu	Pro	Thr	Thr	Gly
			20					25					30		
Arg	Ala	His	Tyr	Asp	Val	Tyr	Ser	Cys	Leu	Pro	Ile	Thr	Leu	Leu	His
		35					40					45			
Leu	Pro	Ala	His	Phe	Gln	Lys	Phe	Ser	Gln	Pro	Ala	Glu	Ile	Ser	His
	50					55					60				
Ile	Arg	Tyr	Arg	Glu	Leu	Leu	Gly	Tyr	Ser	His	Gln	Arg	Pro	Arg	Leu
65					70					75					80
Gln	Lys	Gly	Thr	His	Ser	Ser	Arg	Gln	Val	Ala	Ala	Leu	Pro	Leu	Val
				85					90					95	
Pro	Arg	Ser	Ser	Thr	Leu	Asp	Lys	Tyr	Val	Ala	Phe	Phe	Thr	Ala	Val
			100					105						110	
Phe	Phe	Ile	Leu	Leu	Val	Gly	Ser	Phe	Arg	Phe	Leu	Asp	Val	Ala	Ala
		115					120					125			
Gly	Thr	Lys	Ile	Pro	Leu	His	Leu	Val	Lys	Ser	Leu	Leu	Leu	Ser	Lys
	130					135					140				
Ile	Ser	Lys	Pro	Leu	Glu	Val	Ser	Ser	Ser	Thr	Leu	Phe	Gln	Thr	Phe
145					150					155					160
Leu	Ser	Ala	Asn	Lys	Ile	Ile	Lys	Lys	Gly	Asp	Trp	Lys	Leu	Pro	Tyr
				165					170					175	
Phe	Val	Phe	Leu	Leu	Leu	Gly	Arg	Ile	Ile	Lys	Gly	Glu	His	Pro	Pro
			180					185					190		
Leu	Met	Gly	Leu	Arg	Ala	Ala	Phe	Leu	Ala	Trp	His	Phe	His		
	195						200					205			